

Nutrición Hospitalaria



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OFICINA

Isabel Colbrand, 10-12
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DIRECTOR

JESÚS M. CULEBRAS

De la Real Academia de Medicina y Cirugía de Valladolid y del Instituto de Biomedicina (IBIOMED).
Universidad de León. Investigador colaborador externo, Instituto de Investigaciones Sanitarias
Hospital Universitario Fundación Jiménez Díaz. Ac. Profesor Titular de Cirugía - jesus@culebras.eu

REDACTOR JEFE

A. GARCÍA DE LORENZO Y MATEOS

Jefe del Servicio de Medicina Intensiva. Ac. Catedrático de Universidad. H. U. La Paz.
Paseo de la Castellana, 261. 28046 Madrid. Director de la Cátedra UAM-Abbott de Medicina Crítica. Dpto. de Cirugía. Universidad Autónoma de Madrid - agd@telefonica.net

COORDINADORES DEL COMITÉ DE REDACCIÓN

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ALICIA CALLEJA FERNÁNDEZ

Complejo Asist. Univ. de León (León)
calleja.alicia@gmail.com

CRISTINA CUERDA COMPÉS

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IGNACIO JAUREGUI LOBERA

Universidad Pablo de Olavide (Sevilla)
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ROSA ANGÉLICA LAMA MORÉ

H. U. Infantil La Paz (Madrid)
rlama.hulp@salud.madrid.org

DANIEL DE LUIS ROMÁN

H. U. de Valladolid (Valladolid)
dadluis@yahoo.es

LUIS MIGUEL LUENGO PÉREZ

H. U. Infanta Cristina (Badajoz)
luismluengo@hotmail.com

DAVID MARTÍNEZ GÓMEZ

Instituto del Frio. CSIC (Madrid)
d.martinez@uam.es

J. M. MORENO VILLARES

Hospital 12 de Octubre (Madrid)
jmoreno.hdoc@salud.madrid.org

CONSUELO PEDRÓN GINER

H. I. U. Niño Jesús (Madrid)
consuelocarmen.pedron@salud.madrid.org

MARÍA DOLORES RUIZ LÓPEZ

Universidad de Granada (Granada)
mdruiz@ugr.es

MIGUEL A. MARTÍNEZ OLMOS

C. H. U. de Santiago (Santiago de Compostela)
miguel.angel.martinez.olmos@sergas.es

FRANCISCO J. SÁNCHEZ-MUÑOZ

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frasan@ucom.es

CARMINA WANDEN-BERGHE

Univ. CEU Cardenal Herrera (Alicante)
carminaw@telefonica.net

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Revisión

Adhesion molecules and chemokines: relation to anthropometric, body composition, biochemical and dietary variables

Renata Adrielle Lima Vieira¹, Renata Nascimento de Freitas² and Ana Carolina Pinheiro Volp³

¹Nutrition and Health MSc Student (Research Line: Nutrition Biochemistry and Pathophysiology). Federal University of Ouro Preto, Ouro Preto-Minas Gerais. Brazil. ²PhD in Biochemistry and Immunology and Associate Professor at Federal University of Ouro Preto, Ouro Preto-Minas Gerais. Brazil. ³PhD in Food Science and Technology, and Associate Professor at Federal University of Ouro Preto, Ouro Preto-Minas Gerais. Brazil.

Abstract

Introduction: Among the inflammatory mediators involved in the pathogenesis of obesity, the cell adhesion molecules P-selectin, E-selectin, VCAM-1, ICAM-1 and the chemokine MCP-1 stand out. They play a crucial role in adherence of cells to endothelial surfaces, in the integrity of the vascular wall and can be modulated by body composition and dietary pattern.

Objectives: To describe and discuss the relation of these cell adhesion molecules and chemokines to anthropometric, body composition, dietary and biochemical markers.

Methods: Papers were located using scientific databases by topic searches with no restriction on year of publication.

Results: All molecules were associated positively with anthropometric markers, but controversial results were found for ICAM-1 and VCAM-1. Not only obesity, but visceral fat is more strongly correlated with E-selectin and MCP-1 levels. Weight loss influences the reduction in the levels of these molecules, except VCAM-1. The distribution of macronutrients, excessive consumption of saturated and trans fat and a Western dietary pattern are associated with increased levels. The opposite could be observed with supplementation of w-3 fatty acid, healthy dietary pattern, high calcium diet and high dairy intake. Regarding the biochemical parameters, they have inverse relation to HDL-C and positive relation to total cholesterol, triglycerides, blood glucose, fasting insulin and insulin resistance.

Conclusion: Normal anthropometric indicators, body composition, biochemical parameters and eating pattern positively modulate the subclinical inflammation that results from obesity by reducing the cell adhesion molecules and chemokines.

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Key words: Cell adhesion molecules. Inflammation. Body composition. Anthropometry. Dietary habits.

Correspondence: Ana Carolina Pinheiro Volp.
Department of Clinical and Social Nutrition.
Nutrition School. Federal University of Ouro Preto.
Campus Universitário.
Morro do Cruzeiro, s/n.
CEP 35.400-000 Ouro Preto. Minas Gerais. Brazil.
E-mail: anavolp@gmail.com

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MOLÉCULAS DE ADHESIÓN Y QUIMIOCINAS; RELACIÓN CON VARIABLES ANTROPOMÉTRICAS, DE COMPOSICIÓN CORPORAL, BIOQUÍMICAS Y DIETÉTICAS

Resumen

Introducción: Entre los mediadores inflamatorios involucrados en la fisiopatología de la obesidad, se destacan las moléculas de adhesión P-selectina, E-selectina, VCAM-1, ICAM-1 y la quimiocina MCP-1. Estas desempeñan un papel crucial en la adherencia de células en las superficies endoteliales y en la integridad de la pared vascular y pueden ser moduladas por la composición corporal y patrón alimentario.

Objetivos: Describir y discutir la relación de esas moléculas de adhesión y quimiocina con marcadores antropométricos, composición corporal, bioquímicas y dietéticas.

Métodos: Se utilizaron bases científicas electrónicas para selección de artículos, sin límite de año de publicación.

Resultados: Todas las moléculas se asociaron de forma positiva con marcadores antropométricos; sin embargo, se encontraron resultados controvertidos para ICAM-1 y VCAM-1. No solamente la obesidad per se, sino también la grasa visceral está más fuertemente relacionadas con las concentraciones de E-selectina y MCP-1. La pérdida de peso influencia en la reducción de las concentraciones de esas moléculas, con excepción de la VCAM-1. La distribución de macronutrientes, el consumo excesivo de grasa saturada y trans y un patrón alimentario occidental están asociados con aumento de sus concentraciones. El inverso se pudo observar con la suplementación de ácido graso w-3 en la dieta, el patrón alimentario sano y dieta rica en calcio y productos lácteos. Ya en cuanto a los parámetros bioquímicos, las mismas poseen relación inversa con HDL-c y positiva con colesterol total, triacilglicérols, glicemia e insulinemia de ayuno y resistencia a insulina.

Conclusión: Marcadores antropométricos, composición corporal, parámetros bioquímicos y patrón alimentario adecuados modulan positivamente la inflamación subclínica derivada de la obesidad por medio de la reducción de las moléculas de adhesión y quimiocinas.

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Palabras clave: Moléculas de adhesión celular. Inflamación. Composición corporal. Antropometría. Hábitos Alimenticios.

Abbreviations

BMI: Body mass index.
CAMs: Cell adhesion molecules.
CCL2: Chemokine ligand 2.
CVD: Cardiovascular disease.
HDL-c: High-density lipoprotein.
HOMA-IR: Homeostatic model assessment insulin resistance.
ICAM-1: Intercellular adhesion molecule-1.
IFN- γ : Interferon γ .
IL4: Interleukin 4.
IL6: Interleukin 6.
IL8: Interleukin 8.
IL1: Interleukin 1.
IR: Insulin Resistance.
LDL-c: Low-density lipoprotein.
MCP-1: Monocyte chemoattractant protein-1.
MS: Metabolic syndrome.
ROS: Reactive oxygen species.
T2DM: Type 2 Diabetes Mellitus.
TNF- α : Tumor necrosis factor- α .
VCAM-1: Vascular adhesion molecule-1.
WC: Waist circumference.
WHR: Waist-hip ratio.

Introduction

Obesity is a complex disease of multifactorial causes that is growing exponentially worldwide,¹ defined as excessive accumulation of body fat to such an extent that is detrimental to health.²

Studies show the relation between obesity and subclinical inflammation.^{3,4} This process is related to expansion of adipocytes and infiltration of macrophages into adipose tissue, where there is an increased secretion of pro-inflammatory cytokines such as interleukin-6 (IL-6), IL-8, tumor necrosis factor (TNF- α), complement C3 and monocyte chemoattractant protein-1 (MCP-1).⁵⁻⁸ These pro-inflammatory cytokines can also substantially affect insulin sensitivity and endothelial dysfunction, as well as stimulate a proliferative response in the vascular wall, which clearly promotes an increased risk for type 2 diabetes (T2DM) and cardiovascular diseases (CVD).^{9,10}

When endothelial dysfunction occurs due to an exposure to an activation stimulus such as modified lipoproteins, pro-inflammatory cytokines or coagulation cascade proteases like thrombin, induction and expression of cell adhesion molecules (CAMs) on the surface of the endothelium increasing their interaction with circulating leukocytes can occur. Among them, we highlight the vascular cell adhesion molecule-1 (VCAM-1), the intercellular adhesion molecule-1 (ICAM-1), members of the selectin family (P-selectin and E-selectin) and MCP-1 chemokine.^{11,12}

Studies indicate high levels of circulating CAMs in obesity, especially in obesity characterized by accumu-

lation of visceral adipose tissue.^{9,13,14} However, studies linking these molecules and anthropometric markers of obesity are still controversial and inconclusive.¹⁵⁻²⁰ For some molecules, weight loss in obese individuals, whether achieved by dietary or surgical intervention, has positive relation to their levels,^{18,21,22} but unlike it was expected, Keogh et al.²³ observed a small but significant increase in VCAM-1 after 8 weeks of dietary intervention, which demonstrates that other factors may be involved in the reduction of these concentrations.

In parallel, the connection between dietary patterns and effects on inflammatory response, and consequently, on levels of CAMs and chemokines has been discussed.^{21,24,25} Diet macronutrient distribution and the amount of micronutrients can affect oxidative stress and cause inflammatory changes, which together with a model of chronic excessive intake could induce a pro-inflammatory process.^{25,26} High calcium diets, for example, can reduce levels of MCP-1.²⁷ In addition, components of the diet such as trans fatty acids and high glycemic load are considered pro-inflammatory, while a suitable ratio of ω -3 and ω -6 polyunsaturated fatty acids is considered anti-inflammatory.^{21,26,28,29} On the other hand, low-calorie diets have contradictory relation to levels of cell adhesion molecules. For P-selectin and ICAM-1,^{22,30} such diets have positive influence reducing their levels, while VCAM-1 levels can increase depending on macronutrients distribution.²³

Similarly, the relation of cell adhesion molecules and biochemical parameters such as fasting glucose, insulinemia, triglycerides, total cholesterol and fractions and presence of metabolic syndrome (MS) is also not fully elucidated and for some molecules, such relations are rare.^{17,31,32,33}

In this context, the objective of this review was to describe and discuss the role of P-selectin, E-selectin, ICAM-1, VCAM-1 and MCP-1 in inflammation and their relation to anthropometric, body composition, dietary and biochemical markers.

Methods

This review was conducted using electronic scientific databases, including Medline, PubMed and SciELO, using the following key words in English, Spanish and Portuguese: inflammation, obesity, cell adhesion molecules, VCAM-1, ICAM-1, E-selectin, P-selectin, CCL2 and MCP-1 chemokines, adipose tissue, anthropometry, body composition, diet(ary) pattern. The articles were selected after reading the abstract and regardless of their year of publication.

Obesity and inflammation

Obesity is the most prevalent chronic metabolic disease in the world. In 2005, over 1.6 billion adults

were overweight, of which at least 400 million were obese.³⁴ This disease results from a positive energy balance in med/long term. Excess energy is stored in adipose tissue and, if this process is prolonged, the individual develops obesity. The balance between food intake and energy expenditure is influenced by a complex interaction of genetic, environmental and social factors³⁵ and it is associated with numerous comorbidities that affect individuals life quality, such as T2DM, CVD and some types of cancers.³⁶

Obese individuals may develop insulin resistance (IR) and MS, and these changes may lead to T2DM. Not only excess body fat, but distribution and type of body fat exert different effects. Evidence has shown a causal relation between obesity and T2DM due to the fact that visceral adipose tissue is more metabolically active than subcutaneous and gluteal-femoral adipose tissue, causing increased production of free fatty acids, IR, hyperglycemia and consequently hyperinsulinemia⁹. Moreover, infiltration of inflammation-related cytokines and white adipose tissue immune cells produces a chronic low-grade inflammation and it is, in part, responsible for the pathogenesis of insulin resistance in obese.^{4,37}

Adipocyte hypertrophy that occurs in obesity causes an increased production of a number of pro-inflammatory cytokines and chemokines by the same cells and stromal vascular cells, such as TNF- α , IL-6, IL-1 β , resistin, MCP-1, among others.^{5,6,7,10} The increased production of these molecules triggers local effects on the endothelium, leading to an increased production of CAMs and vascular permeability, which ultimately are translated into an increase in monocyte infiltration and accumulation of macrophages.^{7,9} Thus, the mechanism by which obesity may trigger a chronic inflammatory process is clear.

However, the inverse relation has been suggested, that is, obesity as a consequence of chronic inflammation, also known as subclinical.^{3,38,39} According to Das³⁸ and Engström et al.,³⁹ inflammatory cytokines IL-6, IL-1 β and TNF- α are involved in metabolism regulation and food intake by regulating insulin action in adipose tissue and modulating release of leptin by this tissue, and these effects can be enhanced by the polymorphism of the TNF- α receptor-2 gene that is associated with leptin resistance and obesity. Thus, it is believed to be a vicious cycle between obesity and inflammation induced by changes in adipose tissue.⁴⁰

Migration of leukocytes in inflammatory response

The inflammatory response is the body's first defense against tissue damage which aims to remove the response inducing stimulus and to initiate local tissue recovery. This response is coordinated by cellular mediators categorized according to their biochemical properties, such as vasoactive amines, vasoactive peptides, lipid mediators, cytokines, chemokines and proteolytic enzymes.⁴¹

Initially, after tissue damage caused by injury or infection, there is a production of inflammatory mediators such as IL-1 β , TNF- α and IL-6, chemokines, as well as the expression of CAMs that produce exudate composed of large molecules as albumin and fibrinogen. After that, other plasma proteins migrate to the extravascular space together with leukocytes, which start to circulate along the endothelium through the post-capillary venules.⁴² These changes support a key role of activated vascular endothelium, which is to promote the mobilization and recruitment of leukocytes to the inflammatory site.⁴³

The migration of leukocytes into tissues depends on the binding that occurs between these cells and CAMs. Then, signals within the endothelial cells are activated, allowing the opening of narrow vascular passages that are small intercellular gaps. The movement of leukocytes through these passages is stimulated by chemokines produced by the endothelium and tissue. The majority of these cells migrate through these intercellular gaps, but in severe inflammation conditions, a small percentage of leukocytes can transcellular migrate.⁴⁴

The leukocytes migration process into the extravascular space during inflammatory response is regulated by reactive oxygen species (ROS). This process, known as adhesion cascade, involves some steps that typically include: rolling of leukocytes on the endothelial cell surface followed by arrest of leukocytes on the endothelium for adhesion and high affinity and subsequent transmigration into the inflammation tissue site (fig. 1).^{43,45}

The rolling leukocytes express integrins in a low affinity that, after being activated by chemokines produced by activated vascular endothelium, lead to increased affinity. Subsequently, integrins stabilize selectin-mediated binding, reduce the rolling speed favoring the adhesion of leukocytes to the endothelium and promote their passage from the blood to the tissues.⁴⁶

The transient and reversible interactions of leukocytes rolling on the endothelium are mediated by weak binding between selectins propagated on the endothelium and on leukocytes and by a firm adhesion interceded primarily by VCAM-1 and ICAM-1, which bind to integrins 1 and 2 expressed on leukocytes.^{47,48}

If inflammatory response persists, qualitative changes, characterized by replacement of leukocytes by macrophages and chronicity of the process, occur. The chronicity of the inflammatory state is a matter of scientific research since little is known about causes and mechanisms involved in such state and its involvement in development of chronic diseases.⁴⁹

Cell Adhesion Molecules (CAMs)

The CAMs are membrane receptors glycoproteins that play an important role in the adhesion of cells to extracellular matrices and to endothelial surfaces⁵⁰.

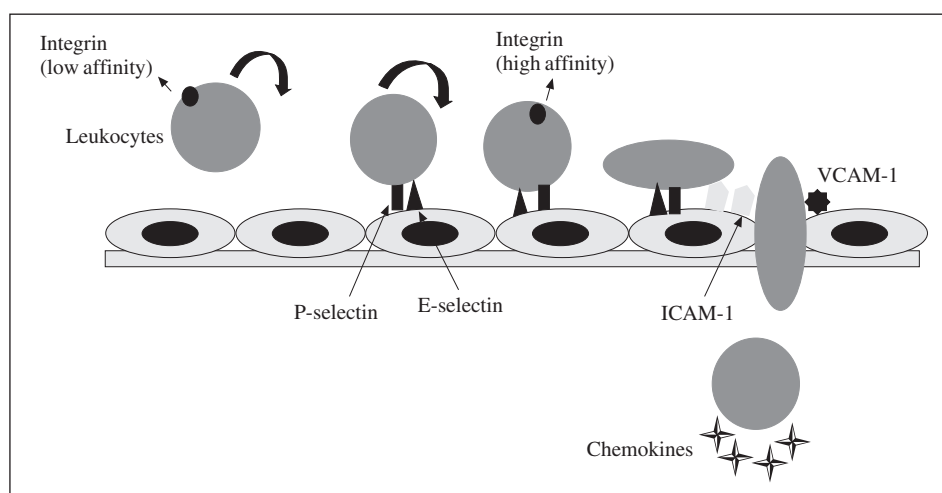


Fig. 1.—Leukocytes migration process. The rolling leukocytes express integrins of low affinity that, after their activation by chemokines, acquire high affinity for endothelial cells. Then the selectin mediated binding is stabilized, the rolling speed is reduced, promoting leukocyte adhesion to vascular endothelium interceded by VCAM-1 and ICAM-1 and promoting the opening of intercellular passages, allowing leukocytes to pass from blood to tissues.

They are known to mediate cell-endothelium interactions of leukocytes and platelets with a critical role in many processes, including inflammation and vascular wall integrity, in addition to being essential for maintaining health and being involved in development of chronic diseases.⁵¹

Based on their structure and role, CAMs can be divided into three main families: integrins, selectins and immunoglobulin superfamily. Among them, P-selectin, E-selectin, ICAM-1 and VCAM-1 are relevant in chronic inflammatory process, and therefore have a prominent role in CVD.^{41,52,53} The distribution and roles of these molecules in the inflammatory process are presented in table I.

Selectins

Selectins are binding protein molecules that mediate the initial low affinity interaction between leukocytes

and endothelial cells and manifest as rolling leukocytes. This transient binding, despite the low affinity, results in increased leukocyte recruitment to the periphery and subsequent firm adhesion and transendothelial migration of these cells.⁴¹

In contrast to most of the other CAMs, the role of selectins is restricted to interactions between leukocytes and vascular endothelium, and P-selectin and E-selectin are the most important molecules in this process. Soluble forms of selectins can be detected in plasma, where high concentrations have been reported in animals and patients with inflammatory diseases.⁵⁵

P-Selectin

P-selectin is identified and stored in alpha granules of platelets and in Weibel-Palade bodies of endothelial cells from where it can be rapidly mobilized to the cell

Table I
Adhesion molecules and chemokine: their cellular role and distribution

<i>Adhesion molecules/chemokine</i>	<i>Distribution</i>	<i>Role</i>
P-selectin	Platelets, endothelium	Interaction between platelets and endothelium, adhesion, rolling and recruitment of leukocytes to the endothelium
E-selectin	Endothelium	Adhesion, rolling and recruitment of leukocytes to the endothelium
VCAM-1	Endothelium, mild atherosclerotic injury in muscle cells	Adhesion of leukocytes to endothelial cells
ICAM-1	Endothelium, leukocytes, fibroblasts, mild atherosclerotic injury in muscle cells	Adhesion and transmigration of leukocytes
MCP-1	Epithelial, endothelial and immune cells	Leukocyte recruitment

ICAM-1: Intercellular adhesion molecule-1; VCAM-1: Vascular adhesion molecule-1; MCP-1: Monocyte chemoattractant protein-1. Adapted from Hope and Meredith⁵⁰ and Calder et al.⁵⁴

surface in response to a variety of inflammatory agents such as cytokines and free radicals.^{53,56}

The expression of P-selectin on the surface of endothelial cells is usually of short duration, so this makes it an ideal candidate for mediating early leukocyte-endothelial interactions. It has an agile kinetics that reveals its important role in recruitment of neutrophils in the early stages of inflammatory reaction.⁵⁷

Few studies have reported high concentrations of P-selectin in the plasma of obese patients^{22,58} and its relation to fat distribution has not been well established. Its concentration is directly related to body mass index (BMI), waist-hip ratio (WHR) and waist circumference (WC).^{22,59,60} However, Pou et al.⁵⁹ showed that both visceral and abdominal subcutaneous fat have also been associated with P-selectin concentrations. When adjusted for BMI and WC, though, this relation did not remain significant (table II). Thus, this suggests that the relation between P-selectin and visceral adiposity is independent of BMI and WC. This is probably justified by the fact that BMI does not assess obesity itself, understood as excess adipose tissue and WC, used in clinical practice as a marker of visceral fat, also takes into consideration the abdominal subcutaneous fat. Therefore, obese patients may not have very representative visceral fat, proportionally, in relation to total fat and consequently maintain homeostasis in relation to inflammatory process.

Weight loss is a method that is likely to improve concentrations of inflammatory markers and endothelial dysfunction in obese subjects. Thus, the kind of intervention, dietary or surgical, can influence the reduction of P-selectin concentrations. Roberts et al.⁶¹ studying weight loss in obese men after 3 weeks and Ziccardi et al.²² in obese women after one year, both resulting from dietary intervention and physical activity, showed decreased P-selectin concentrations (table III). This decrease was also observed after the fourth month of weight loss following surgery in morbidly obese⁶². This is possibly due to reduction of adiposity, which results in improved endothelial activation and is related to reduction of this adhesion molecule.

However, it is unclear whether diets varying in macronutrient composition can affect inflammatory responses differently. Sharman and Volek³⁰ compared a low calorie diet with very low carbohydrate levels (< 10% carbohydrate) and low fat levels (25% fat, < 10% saturated fat and < 300 mg cholesterol) on inflammatory markers in overweight men. After 6 weeks of intervention there was no significant reduction in absolute concentration of P-selectin for both diets. However, when inflammatory values were normalized with reduction of 1 kg of body weight, there was a significant reduction of P-selectin for both treatments and it was higher for the very low carbohydrate level diet (table IV). The results of this study suggest that in a short period of time, weight loss and not diet composition seems to be the underlying driving force in reducing these inflammatory markers.

Besides adiposity and macronutrient composition, biochemical parameters also influence concentrations of CAMs. Studies have shown that concentrations of P-selectin were positively associated with fasting glucose,¹⁷ triglycerides and total cholesterol and inversely associated with high-density lipoprotein (HDL-c)^{16,60} in apparently healthy individuals. This association of triglycerides and HDL-c was found by Miller and Cappuccio¹⁹ after adjustment on age and sex (table V).

This way, it is becoming clear that P-selectin is an essential component in cardiovascular disease and therefore is a potential therapeutic target. A longitudinal monitoring of apparently healthy women for 3.5 years showed that concentrations of P-selectin were significantly higher in the beginning of the study among participants who subsequently developed a first cardiovascular event than those who had no event. In this study, relative risk of future events increased by 25% for each quartile increase in basal level of P-selectin.⁶³

Therefore, concentrations of P-selectin are directly related to obesity markers and weight loss. However, as to body composition, unlike what was expected, its relation is not yet well established, since there was no association of P-selectin with visceral or subcutaneous fat. The macronutrient distribution or a healthy eating pattern also need to be elucidated, since studies indicate a reduction in concentrations of P-selectin resulting from weight loss induced by diet and not due to its composition. Similarly, the relation of this molecule with biochemical parameters should be more studied, since these are all contributing factors to cardiovascular events through its inflammatory effects on vascular endothelium.

E-Selectin

E-selectin is expressed on endothelial cells specifically and strongly stimulated by inflammatory molecules such as TNF- α and IL-1 β , and it is widely expressed in vasculature on sites of inflammation.⁶⁴

Its relation to the occurrence and type of obesity, as well as to anthropometric markers is established. The concentrations of E-selectin were significantly associated with BMI and WHR.^{16,17,19,33} When compared, the concentrations of E-selectin in obese and nonobese individuals, they are significantly higher in obese, and visceral obesity is more strongly related than total fat.^{14,33} This could be explained by production of TNF- α and IL-6 derived from visceral adipocytes on which they induce increased expression of this molecule.³³

Studies also point to reduction in concentrations of E-selectin with weight loss, whether due to dietary or surgical intervention. Ito et al.¹⁸ when studying obese women after 3 months of nutritional intervention and physical activity, showed a significant reduction of this molecule. Similar results were found by Pontiroli et

Table II
Association of adhesion molecules and chemokine with anthropometric markers and body composition

<i>Subject</i>	<i>n (sex)</i>	<i>Type of study</i>	<i>Methods</i>	<i>Association</i>	<i>Reference</i>
Obese	56(M)	Transversal	Sedentary individuals. Anthropometric and body composition data were collected. This by computed tomography.	BMI: ↑ E-selectin, ICAM-1, ↔ VCAM-1 WC: ↔ E-selectin, ICAM-1, ↑ VCAM-1 WHR: ↑ E-selectin, VCAM-1, ↔ ICAM-1 SAT: ↔ E-selectin, VCAM-1, ↑ ICAM-1 VAT: ↑ E-selectin, VCAM-1, ↔ ICAM-1	14
Healthy	316 (M/F)	Cohort	Monitoring of medical history, smoking, alcohol consumption and anthropometry over 5 years.	BMI: ↑ E-selectin, ↔ ICAM-1, VCAM-1	15
Healthy	592 (M/F)	Transversal	Evaluated lifestyle and anthropometry.	WHR: ↑ P-selectin, E-selectin, ICAM-1, VCAM-1	16
Healthy	493 (M/F)	Transversal	Evaluated lifestyle and anthropometry.	BMI: ↑ P-selectin, E-selectin, ICAM-1	17
Obese	46 (M)	Transversal	Consisted of a 3 month follow-up with lectures on diet, exercise and behavioral modification.	BMI, WC: ↑ E-selectin, ICAM-1	18
Healthy	664 (M/F)	Transversal	Individuals of different ethnicities. Evaluated clinical and anthropometric parameters.	BMI: ↑ E-selectin, ↔ P-selectin, ICAM-1, VCAM-1 WHR: ↑ E-selectin, ICAM-1, VCAM-1, ↔ P-selectin	19
Healthy	1577 (M/F)	Transversal	Different ethnic groups, conducted anthropometric, biochemical and clinical measures.	BMI: ↑ E-selectin, ↔ P-selectin, ICAM-1, VCAM-1 WHR: ↑ E-selectin, ICAM-1, VCAM-1, ↔ P-selectin	20
Obese and non obese	96 (F)	Transversal	Dietary intervention and exercise over 12 months and liposuction for women candidates.	BMI: ↑ P-selectin, VAM-1, ICAM-1 WHR: ↑ P-selectin, VAM-1, ICAM-1	22
Obese and non obese	100 (M/F)	Transversal	Conducted medical evaluation, physical examination and anthropometry.	BMI, WC: ↑ MCP-1	31
Obese and non obese	87 (M/F)	Transversal	Conducted anthropometric measures and body composition by computerized tomography.	BMI, WHR, VAT: ↑ E-selectin SAT: ↔ E-selectin	33
Healthy	1250(M/F)	Transversal	Conducted anthropometric measures and body composition by computerized tomography.	BMI: ↑ P-selectin, ICAM-1, MCP-1 WC: ↑ P-selectin, ICAM-1, MCP-1 SAT: ↔ P-selectin, ICAM-1, MCP-1 (after adjustment for BMI and WC) VAT: ↔ P-selectin, ICAM-1, MCP-1 (after adjustment for BMI and WC)	59
Healthy	3013 (M/F)	Transversal	Monitored by Framingham and Omni Study, through medical history and lifestyle habits.	BMI: ↔ P-selectin, ICAM-1, ↑ MCP-1 WC: ↑ P-selectin, ↔ ICAM-1, MCP-1	60
Healthy	27.158 (M)	Transversal	Evaluated anthropometric data, lifestyle and physical activity.	BMI: ↑ ICAM-1	75
Healthy	145 (M)	Transversal	Women without breast cancer. Anthropometric measures and biochemical parameters were evaluated.	BMI: ↔ ICAM-1, ↓ VCAM-1 WHR: ↔ ICAM-1, VCAM-1	81
Obese mice	40	Transversal	Obesity was induced by high lipid diet from the time they were 9 weeks old.	Adiposity: ↑ MCP-1	91
Obese and non obese	20 (M/F)	Transversal	Individuals were submitted to surgery, and the obese were submitted to placement of adjustable silicone gastric band by laparoscopy. From this, adipocytes were isolated.	BMI, VAT: ↑ MCP-1	92
Obese	90 (M/F)	Cohort	Adipose tissue was obtained by biopsy performed in volunteers undergoing abdominal surgery for gastric banding, gastric weight reduction surgery, or laparotomy.	VAT: ↑ MCP-1	93
Obese	23 (M/F)	Transversal	Lifestyle intervention for 12 weeks consisting of hypocaloric diet combined with physical activities for at least 2 hours/day.	BMI: ↑ MCP-1	94
Obese and non obese mice	12	Transversal	Knockout mice for the MCP-1 receptor were put on a high fat diet to determine obesity.	Adiposity: ↑ MCP-1	95

↑ positive association; ↔ no association; ↓ negative association; ICAM-1: Inter cellular adhesion molecule-1; VCAM-1: Vascular adhesion molecule-1; MCP-1: Monocyte chemoattractant protein-1; BMI: body mass index; WC: waist circumference; WHR: waist-hip ratio; SAT: subcutaneous adipose tissue; VAT: visceral adipose tissue; M- male; F: female.

Table III
Effect of weight loss on adhesion molecules and chemokine

Subject	n (sex)	Intervention period	Methods	Effect	Reference
Obese	46 (F)	3 months	Consisted of lectures on diet, exercise sessions and behavioral modification. Emphasis on themes of calorie restriction, increasing consumption of vegetables and grains and replacing saturated fats with unsaturated.	↓ E-selectin, ICAM-1	18
Obese and non obese	96 (F)	12 months	Intervention with hypocaloric diet, exercise and liposuction for women candidates. Diet composition: 1300 kcal, 55% carbohydrate, 22% protein, 23% fat and 25 g fibers.	↓ P-selectin, VCAM-1, ICAM-1	22
Obese	99 (M/F)	8 weeks	Intervention with two types of hypocaloric diet: a low-carbohydrate and high in saturated fat (4% carbohydrate, 61% lipid, 20% saturated fat) and low in saturated fat (46% carbohydrate, 30% lipid, < 8% saturated fat).	↓ P-selectin, E-selectin, ICAM-1 ↑ VCAM-1	23
Obese and SM	31 (M)	3 weeks	Dietary intervention and daily exercise. Diet: 12-15% fat, 15-20% protein and 65-70% mainly from complex carbohydrates, > 40 g of dietary fiber.	↓ P-selectin, ICAM-1	61
Morbid obese and non obese	49 (M/F)	4 months	Weight loss was due to bariatric surgery.	↓ P-selectin, E-selectin, VCAM-1, ↔ ICAM-1	62
Obese and non obese	126 (M/F)	12 months	The intervention was adjustable gastric band or diet and physical activity. Hypocaloric diet: 1000 for men and 1100 kcal / day for women, 48% carbohydrate, 33% protein and 19% fat (olive oil).	↓ E-selectin, ICAM-1	65
Obese mice	40	18 weeks	Weight loss was due to feed restriction.	↓ MCP-1	91
Obese	23 (M/F)	12 weeks	Intervention with low-calorie diet combined with physical activity for at least 2 hours/day.	↓ MCP-1	94

↑ increased; ↔ no effect on; ↓ decreased; ICAM-1: Inter cellular adhesion molecule-1; VCAM-1: Vascular adhesion molecule-1; MCP-1: Monocyte chemoattractant protein-1; CHO: carbohydrate; PTN: protein; LIP: lipid; M- male; F: female.

al.⁶⁵ in surgical weight loss in individuals with morbid obesity. This suggests a reduction of endothelial activation and an important role of adipose tissue in this pathophysiological mechanism.

Diet macronutrient composition can directly affect concentrations of E-selectin. When comparing different meals overloaded with glucose, fat or in combination, in healthy individuals, it was found an increase in these levels after high fat and glucose meals, and when combined, there were more pronounced effects on E-selectin.²¹ This increase is due to hyperglycemia and postprandial hypertriglyceridemia, which have independent but cumulative effects and promote an atherogenic profile.

Moreover, a healthy dietary pattern, characterized by consumption of fruits, vegetables, fish, poultry and whole grains was associated with decreased concentrations of E-selectin after adjustment for age, BMI, physical activity, smoking and alcohol consumption in apparently healthy women. At the same time, a Western dietary pattern characterized by higher intakes

of red meat, sweets, fries and refined grains was associated with increase in these concentrations.^{66,67}

The type of lipid in the diet may also differentially influence endothelial activation. The w-3 alpha-linolenic fatty acid consumption in overweight individuals with hypercholesterolemia significantly reduces E-selectin concentrations, since it activates mechanisms that beneficially affect both lipids/lipoproteins and CAMs on which they inhibit endothelial activation⁶⁸. The intake of trans fatty acids is directly associated with increased concentrations of E-selectin, due to vasodilatation, and consequent increase of CAMs and reduced HDL-c, which can cause oxidation of low density lipoproteins (LDL-c). This indicates that dietary factors may influence the cardiovascular risk through modulation of endothelial function.²⁴

The concentrations are also related to biochemical parameters. Fasting glucose, fasting insulin and triglycerides were positively associated with E-selectin,^{17,19,33} while HDL-c had a negative association^{19,33} in healthy individuals. As for individuals with

Table IV
Qualitative and quantitative effect of diet on adhesion molecules and chemokine

<i>Subject</i>	<i>n (sex)</i>	<i>Intervention period</i>	<i>Methods</i>	<i>Effect</i>	<i>Reference</i>
Type 2 diabetics and healthy	50 (M/F)	4 weeks	All participants ate three different diets on different days: a high fat meal (75g fat, 5 g of carbohydrate and 6g of protein per m ² of body surface), a meal with only 75 g of glucose and the third meal was rich in fat and contained 75 g of glucose. Blood samples were collected at 0, 1, 2, 3, and 4 h.	High fat diet: ↑ E-selectin, VCAM-1, ICAM-1 High glucose diet: ↑ E-selectin, VCAM-1, ICAM-1 High fat and glucose diet: ↑ E-selectin, VCAM-1, ICAM-1 (more pronounced than isolated diets)	21
Healthy	730 (F)	Transversal	Food intake was registered using a validated semiquantitative FFQ. Detailed information about the type of fat or oil used for frying (cooking and table), brand, type and year of consumption of margarine.	Intake of trans fatty acids: ↑ E-selectin, VCAM-1, ICAM-1	24
αP2-agouti transgenic mice	30 (M)	3 weeks	Mice were divided into three groups with different diets: one group on control diet (0.4% calcium carbonate), one group with a high concentration of calcium (1.2% calcium carbonate) and the third group consumed a high calcium diet derived from dairy products (1.2% nonfat dry milk).	Diet rich in calcium and dairy: ↓ MCP-1	27
Overweight	15 (M)	6 weeks	Comparison of two hypocaloric diets: a very low-carb diet (< 10% carbohydrate, 60% of fat and 30% of protein) and a low-fat diet (20% protein, 25% fat, < 10% saturated fat and < 300 mg cholesterol, 55% carbohydrate). All volunteers consumed both diets.	Low-carb diet: ↔ P-selectin, ↓ ICAM-1 Low-fat diet: ↔ P-selectin, ↓ ICAM-1	30
Healthy	732 (F)	Transversal	Healthy dietary pattern was characterized by higher intake of fruits, vegetables, fish, poultry and whole grains, and Western dietary pattern was characterized by higher intake of red and processed meats, sweets, desserts, fries and refined grains.	Healthy dietary pattern: ↓ E-selectin, ↔ VCAM-1, ICAM-1 Western dietary pattern: ↑ E-selectin, VCAM-1, ICAM-1	66
Healthy	486 (F)	Transversal	Healthy dietary pattern: rich in fruits, vegetables, tomatoes, poultry, tea, fruit juices and whole grains. Western dietary pattern: rich in refined grains, red meat, butter, processed meats, high fat dairy products, sweets and desserts, pizza, potatoes, eggs, hydrogenated fats and sodas.	Healthy dietary pattern: ↓ E-selectin, VCAM-1, ICAM-1 Western dietary pattern: ↔ E-selectin, ↓ VCAM-1, ICAM-1	67
Hypercholesterolemic individuals	23 (M/F)	6 weeks	Three diets: a standard diet (13% saturated, 13% MUFA and 9% PUFA), a diet rich in PUFA and ALA (8% saturated, 12% MUFA and 17% PUFA) and a diet rich in PUFA and LA (8 % saturated, 12% MUFA and 16% PUFA).	Diet Rich in ALA: ↓ E-selectin, VCAM-1, ICAM-1 more pronounced than the other diets	68
Overweight and obese	11 (M/F)	6 hours after eating	Subjects consumed three high-fat shakes: one rich in saturated fat, the other rich in monounsaturated and the third rich in w-3 polyunsaturated fat. Blood samples were collected at 0, 1, 2, 4 and 6 after eating.	High in saturated fat: ↑ VCAM-1, ↔ ICAM-1 High in monounsaturated: ↔ VCAM-1, ICAM-1 High in polyunsaturated: ↔ VCAM-1, ICAM-1	76
Individuals with coronary artery disease	60 (M/F)	6 weeks	Individuals divided into three groups fed with 700 g/week of Atlantic salmon in different ways: the first with 100% fish oil, the second with 100% canola oil and the third with 50% of each oil, resulting in fillets with high, medium and low levels of w-3 PUFAs.	Fish oil: ↓ VCAM-1 compared with the other oils	82
Obese and non obese mice	12	Transversal	Knockout mice for the receptor of MCP-1 were fed a high saturated fat diet.	High intake of saturated fat: ↑ MCP-1	95

↑ increased; ↔ no effect on; ↓ decreased; ICAM-1: Intercellular adhesion molecule-1; VCAM-1: Vascular adhesion molecule-1; MCP-1: Monocyte chemoattractant protein-1; FFQ: food frequency questionnaire; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids; ALA: α-linolenic acid; LA: linoleic acid; CHO: carbohydrate; PTN: protein; LIP: lipid; M- male; F: female.

Table V
Association of biochemical parameters, adhesion molecules and chemokine

<i>Subject</i>	<i>n (sex)</i>	<i>Type of study</i>	<i>Association</i>	<i>Reference</i>
Obese	56(M)	Transversal	E-selectin: ↑ total cholesterol, triacylglycerols, LDL-c, fasting insulin, HOMA, ↔ HDL-c, fasting blood glucose ICAM-1, VCAM-1: ↔ total cholesterol, triacylglycerols, LDL-c, fasting insulin, HOMA, HDL-c, fasting blood glucose	14
Healthy	316 (M/F)	Cohort	E-selectin: ↑ triacylglycerols, ↔ LDL-c, ↓ HDL-c ICAM-1, VCAM-1: ↔ triacylglycerols, LDL-c, HDL-c	15
Healthy	592 (M/F)	Transversal	P-selectin, E-selectin, ICAM-1, VCAM-1: ↑ total cholesterol, HDL-c	16
Healthy	493 (M/F)	Transversal	P-selectin, ICAM-1: ↑ triacylglycerols, ↔ fasting blood glucose E-selectin: ↔ triacylglycerols, ↑ fasting blood glucose	17
Obese	46 (F)	Transversal	E-selectin: ↑ triacylglycerols, ↔ total cholesterol, HOMA ICAM-1: ↔ triacylglycerols, total cholesterol, HOMA	18
Healthy	664 (M/F)	Transversal	P-selectin, ICAM-1, VCAM-1: ↑ triacylglycerols, ↔ fasting insulin, ↓ HDL-c E-selectin: ↑ triacylglycerols, fasting insulin, ↓ HDL-c	19
Healthy	1577 (M/F)	Transversal	E-selectin: ↑ total cholesterol, triacylglycerols, fasting insulin, fasting blood glucose, ↓ HDL-c P-selectin: ↔ total cholesterol, triacylglycerols, fasting insulin, ↑ fasting blood glucose, ↓ HDL-c ICAM-1: ↑ total cholesterol, triacylglycerols, ↔ fasting insulin, fasting blood glucose, ↓ HDL-c VCAM-1: ↔ total cholesterol, ↑ triacylglycerols, ↔ fasting insulin, fasting blood glucose, ↓ HDL-c	20
Obese and non obese	100 (M/F)	Transversal	MCP-1: ↔ total cholesterol, triacylglycerols, LDL-c, ↓ HDL-c	31
Individuals with MS	37 (M/F)	Transversal	ICAM-1, VCAM-1: ↑ MS, HOMA-IR	32
Obese and non obese	87 (M/F)	Transversal	E-selectin: ↔ total cholesterol, LDL-c, ↑ triacylglycerols, ↓ HDL-c	33
Healthy	3013 (M/F)	Transversal	P-selectin: ↑ triacylglycerols ICAM-1, MCP-1: ↔ triacylglycerols	60
Obese and non obese	126 (M/F)	Transversal	E-selectin, ICAM-1: ↑ insulin, HOMA	65
Healthy	30 (M)	Longitudinal	E-selectin: ↔ fasting and postprandial blood glucose, fasting and postprandial triacylglycerol, fasting and postprandial insulin ICAM-1: ↔ fasting and postprandial blood glucose, fasting and postprandial triacylglycerol, fasting insulin, ↑ postprandial insulin VCAM-1: ↔ fasting and postprandial blood glucose, fasting triacylglycerol, ↑ postprandial triacylglycerol, ↔ fasting and postprandial insulin	78
Healthy, hypercholesterolemic and hypertriglyceridemic individuals	40 (M/F)	Transversal	E-selectin: ↑ total cholesterol ICAM-1: ↑ total cholesterol, triacylglycerols VCAM-1: ↑ triacylglycerols	83

↑ positive association; ↔ no association; ↓ negative association; ICAM-1: Intercellular adhesion molecule-1; VCAM-1: Vascular adhesion molecule-1; MCP-1: Monocyte chemoattractant protein-1; MS: metabolic syndrome; HOMA-IR: Homeostatic model assessment insulin resistance; LDL-c: low-density lipoprotein; HDL-c: high-density lipoprotein; M- male; F: female.

visceral adiposity, E-selectin is related to hyperinsulinemia and IR,¹⁴ which was expected since this adipose tissue is highly lipolytic and has a late interference in post-insulin receptor mechanisms, resulting in inefficient glucose uptake causing such effects.

Thus, E-selectin, may play a role in atherogenesis model centered on inflammation.⁶⁹ The concentrations were significantly associated with coronary artery disease (OR: 1.54, 95% CI: 1.27-1.86) and occurrence of atherosclerosis of the carotid artery (OR: 1.36, 95%

CI: 1.09-1.70). The risk of coronary artery disease in individuals with high levels of E-selectin was 2.98 times higher (95% CI: 1.74-5.10).¹⁵

Therefore, E-selectin is well grounded as to the occurrence and type of obesity and visceral obesity is strongly related to these concentrations. Similarly weight loss is positively associated with its reduction. Macronutrient distribution, healthy eating pattern and type of lipids are also clearly related to E-selectin, since dietary factors can influence modulation of

endothelial function. Along with these factors, total cholesterol and fractions, triglycerides, fasting insulin and fasting glucose are also associated with E-selectin. Thus, E-selectin can be considered a classic molecule for obesity and cardiovascular risk factors.

The immunoglobulin superfamily (IgSF)

The IgSF is the most abundant family of cell surface molecules, representing 50% of all leukocyte surface glycoproteins.⁷⁰ IgSF members are diverse, comprising soluble and membrane-bound immunoglobulin and monomeric adhesion molecules.⁵⁶

These molecules are expressed on endothelial cell membranes, they are also involved in leukocyte adhesion and are induced by TNF- α , interferon- γ (IFN- γ) and IL-1 β . The main molecules of this family are: ICAM-1 and VCAM-1, which are relevant in chronic inflammatory process, with highlights to CVD.⁵⁶

Intercellular Adhesion Molecule-1 (ICAM-1)

ICAM-1 is a transmembrane glycoprotein that binds to integrins in order to facilitate transmigration of leukocytes through vascular endothelium. Intercellular adhesion function has been attributed to ICAM-1 as a result of this binding capacity. Its expression is regulated by agents such as TNF- α and thrombin.^{70,71,72}

The firm adhesion of leukocytes to the endothelium via ICAM-1 causes an increase in intracellular free Ca²⁺, contractility of myosin and activation of p38 kinase. The activation of these signaling pathways results in extensive remodeling events of the cytoskeleton that alter the contractility of endothelial cells, thereby facilitating transmigration and weakening bindings of junctional adhesion molecules.^{73,74}

Its relation to anthropometric markers has been explored, but with controversial results. A study involving apparently healthy women observed a positive and significant relation between BMI and ICAM-1, and showed that women in the highest BMI quintile had 14% higher concentrations than those in lower quintiles.⁷⁵ As to obese women, a significant positive association with BMI and WHR was found.²² However, Ponthieux et al.¹⁷ and Miller and Cappuccio¹⁹ when studying healthy individuals of different ages and ethnicities, respectively, could not observe significant association with BMI after adjustment for age, sex, smoking status and ethnicity. This may have been observed because BMI does not measure, as it was previously mentioned, body composition, which is common among the adjustment variables.

Regarding body composition, however, both subcutaneous and visceral abdominal fat were not associated with ICAM-1 concentrations, when adjusted for BMI and WC. Thus, the concentration of this molecule also seems to be independent of these two anthropometric

markers.⁵⁹ This shows that there may be alternative mechanisms to alteration of such cell adhesion molecule, besides type of adiposity, as possibly reduction of HDL-c and subsequent oxidation of LDL-c, which can be a risk factor for modification of the endothelium regardless body composition.

Weight loss was related to ICAM-1 concentrations. Ito et al.¹⁸ and Ziccardi et al.²² studied weight loss in obese women submitted to hypocaloric dietary intervention after 3 and 12 months, respectively, and observed a positive association with this molecule. Thus, this suggests an important role of adipose tissue in reduction of endothelial activation.

Not only the caloric value, but also qualitative characteristics of the diet may be associated with concentrations of this molecule and therefore with endothelial activation. Studies with women showed that a dietary pattern characterized by higher intakes of red and processed meats, sweets, desserts, fries and refined grains reduces ICAM-1 concentrations.^{66,67} At the same time, consumption of a high glucose load and fat,²¹ particularly saturated fat⁷⁶ and trans fatty acid²⁴ produces a significant increase in ICAM-1. Thus, it is suggested that inappropriate food intake plays an important role in endothelium functional changes caused by oxidation of LDL-c, which is the initial step in development of atherosclerosis.

Prospective studies indicate ICAM-1 concentrations as a predictor of future cardiovascular events.^{15,77} Biochemical parameters considered risk factors for development of CVD such as total cholesterol, triglycerides and HDL-c were associated with concentrations of this cell adhesion molecule, and HDL-c had an inverse association.^{19,20} Furthermore, ICAM-1 is positively related to insulin, postprandial glucose⁷⁸ and IR.¹⁷

Kressel et al.³² used the homeostasis model assessment for definition of IR (HOMA-IR), and showed that individuals who had HOMA-IR ≥ 5.03 had higher concentrations of this marker when compared with those who had HOMA-IR ≤ 1.32 . Therefore, these results reinforce the idea that associations between systemic and vascular inflammation may help explain predisposition for IR in obese patients.

This way, studies on the relation of ICAM-1 with nutritional and dietary parameters present controversial results for anthropometric markers when adjusted for age, sex, smoking status and ethnicity, and further research is required, particularly related to body composition, in order to elucidate its relation with obesity per se and/or the distribution of body fat. However, this molecule is directly related to weight loss, with inadequate dietary pattern, high intake of saturated and trans fat and biochemical parameters, and has an inverse relation with HDL-c.

Vascular Cell Adhesion Molecule-1 (VCAM-1)

VCAM-1 is a type I transmembrane glycoprotein expressed primarily in activated endothelial cells and

binds mainly to $\alpha 4\beta 1$ integrin which is constitutively expressed on lymphocytes, monocytes and eosinophils.⁷⁹

VCAM-1 can mediate both rolling and firm adhesion. Although it is structurally similar to ICAM-1, VCAM-1 has a unique pattern of regulation. It is not expressed in basal conditions, but is rapidly induced by pro-atherosclerotic conditions.^{47,79} It is induced by IL-4 and high concentrations of ROS oxidized LDL-C.⁸⁰

The relation of VCAM-1 concentrations with anthropometric markers is also controversial. Some researches show a positive correlation with BMI,^{15,16,17,22} WC and WHR,¹⁴ while Miller and Cappuccio¹⁹ did not show any significant results between VCAM-1 and BMI after adjustment for age, sex, smoking status and ethnicity. Recently, Souza et al.⁸¹ observed an inverse correlation between VCAM-1 and BMI, when studying apparently healthy women, and showed that for every increase of 1 kg/m² in BMI, there was a reduction of 1,7 ng/mL in its concentrations. Thus, there is still a gap in understanding the mechanisms that explain pathophysiological changes that make obesity a risk factor for increased CAMs.

Results that point to a decrease in concentrations of VCAM-1 as a result of weight loss are also contradictory. Ziccardi et al.²² demonstrated significant reduction of VCAM-1 after a year of nutritional intervention with low-calorie diet in obese women, while Keogh et al.²³ observed a slight increase (5%) in concentrations for 8 weeks with two types of hypocaloric diet, one low in carbohydrates and high in saturated fat and the other high in carbohydrates and low in saturated fat. Although weight loss reduces adiposity and consequently reduces this molecule, this result may be due to the effect of excess fat or carbohydrate in both diets on endothelial function, since such excesses may cause lipogenesis.

Besides distribution of macronutrients, dietary patterns may also influence concentrations of VCAM-1. Individuals whose diets were based on processed foods, high glycemic index, few fruits and vegetables had significantly higher concentrations than those who had higher intake of fish, poultry, fruits, vegetables and whole grains.^{66,67} Moreover, supplementation of w-3 polyunsaturated fatty acids significantly reduced this molecule in hypercholesterolemic individuals⁶⁸ with coronary artery disease.⁸²

Biochemical parameters show little evidence of the relation with concentrations of VCAM-1 in healthy or obese individuals. Positive association of this molecule with triacylglycerols,⁸³ IR³² and total cholesterol and negative association with HDL-c¹⁶ were observed. Nevertheless, evidences indicate that VCAM-1 is one of the major CAMs involved in atherosclerotic lesions and it is the first CAM to be expressed before the development of atherosclerotic plaques.⁴⁵ Its high concentration increases the risk by 2.8 times for future cardiovascular events.⁸⁴

Therefore, contrary to the expected, some studies show that VCAM-1 may have an inverse relation to BMI and weight loss, which suggests that other factors may be involved in its stimulation and/or depression. However,

dietary factors such as adequate food pattern and supplementation of w-3 polyunsaturated fatty acids positively influence the reduction of its concentrations. Similarly, total cholesterol, triglycerides, and IR show a positive correlation and HDL-C is inversely correlated with this molecule, being this the first CAM to be altered in the development of atherosclerotic plaques.

Chemokines

Chemokines constitute a family of small chemotactic cytokines composed of heparin binding proteins that drive the migration of circulating leukocytes to sites of inflammation or injury.^{85,86} These cytokines not only regulate cell chemotaxis by concentration gradients, but also adhesion.^{87,88}

According to Lezama Asencio,⁸⁸ chemokines are involved in metabolic disorders. The main motivation for examining chemokines is how easily their expression can be documented in disorders associated with leukocyte infiltration.⁸⁹ The monocyte chemotactic protein (MCP-1), also named chemokine ligand 2 (CCL2), is a key chemokine in regulation of migration and infiltration of monocytes/macrophages involved in chronic inflammatory diseases.⁹⁰

Monocyte chemoattractant protein-1 (MCP-1/CCL2)

MCP-1 or CCL2 was the first human chemokine to be discovered. It is produced by many types of cell, including endothelial cells, fibroblasts, epithelial cells, smooth muscle cells, monocytes and microglial cells, constitutively or in response to extracellular stimuli such as oxidative stress, cytokines or growth factors. MCP-1/CCL2 and its receptors play a central role in development of inflammatory responses and are crucial for the recruitment of immune cells to sites of inflammation.⁹⁰

In obese humans and rodents, MCP-1/CCL2 is expressed by adipose tissue and increases proportionally to adiposity.^{6,7,91,92} A study of two independent cohorts with obese individuals showed that concentrations of MCP-1/CCL2 increased with obesity, especially with intra-abdominal visceral fat,⁹³ which is expected since this fat deposit is highly lipolytic. Thus, its concentrations are associated with BMI, visceral fat and WC.^{31,59}

Moreover, its reduction is related to weight loss in individuals with severe obesity. A weight loss of 12% in obese individuals resulted in a reduction of 20% in its concentrations ($p < 0,001$).⁹⁴ Thus, it is suggested the importance of reducing adipose tissue in improvement of endothelial activation.

Simultaneously with changes in anthropometric measures as a result of obesity, MCP-1/CCL2 is negatively correlated with HDL-C and positively with IR. These findings indicate that MCP-1/CCL2 can be a potential candidate linking obesity with metabolic complications, such as atherosclerosis and diabetes.³¹

The relation of MCP-1/CCL2 with diet has been poorly described. In humans, a study by Zemel and Sun²⁷ using diets rich in calcium and dairy products resulted in significant suppression when comparing with low calcium diet. The reason for this is probably because the decrease in intracellular calcium concentration induced by high levels of this nutrient in the diet reduces the synthesis of fatty acid synthase and consequently reduces lipogenesis and increases lipolysis. This is a possible mechanism for the effect of dietary calcium in modulating adiposity. In rats, a high fat diet increases the expression of MCP-1/CCL2. Thus, it is suggested that there is an influence of diet composition on the expression of this chemokine.⁹⁵

MCP-1/CCL2 also plays a key role in the pro-inflammatory pathways in vascular endothelium and development of atherosclerosis, situation in which its concentration is high. By using MCP-1/CCL2 in knockout mice to examine atherosclerosis, studies have shown that the absence of this chemokine significantly reduces deposition of lipids in arteries and formation of atherosclerotic lesions.^{86,90}

This way, the relation of MCP-1/CCL2 with anthropometric markers and body composition is well established, especially with intra-abdominal visceral fat, being reduction in its concentrations influenced by weight loss. In parallel, diets rich in calcium are also related to its concentration, but more studies should be conducted in order to understand if dietary pattern and macronutrient distribution also influence positively the reduction of MCP-1/CCL2 once this chemokine is a strong link between obesity and its metabolic complications.

Conclusion/perspectives

The importance of CAMs and chemokines in subclinical inflammation, which can lead to development of metabolic syndrome, obesity and other chronic diseases, is well understood, being this a bidirectional process.

All molecules reviewed here relate positively with an anthropometric marker as BMI, WC, WHR, but studies also show that there is no relation of ICAM-1 with BMI after adjustment for age, sex, smoking status and ethnicity, while for VCAM-1 there may be an inverse relation, its concentrations may be higher in those with lower BMI. As for the body composition, both E-selectin and MCP-1/CCL2 are positively associated with type of fat, being the visceral one more strongly related to its concentrations. However, for P-selectin, VCAM-1 and ICAM-1, both subcutaneous and visceral abdominal fat were not associated with its concentrations.

Weight loss, whether due to hypocaloric diets with different macronutrient distribution or surgical, influences positively the reduction in concentrations of all CAMs and chemokines studied, except for VCAM-1 in which distribution of macronutrients can influence more than calorie reduction, which suggests that other

factors may be involved in its stimulation and/or depression.

Besides distribution of nutrients, high consumption of trans fatty acids, saturated fat and a Western dietary pattern are associated with increased concentrations of CAMs. In contrast, individuals that supplement w-3 fatty acid in diet, have a healthy dietary pattern and a diet rich in calcium and dairy products and have lower concentrations of these molecules and MCP-1/CCL2.

Regarding biochemical parameters, all molecules and the chemokine have inverse relation of their concentrations with HDL-C and positive relation with total cholesterol and triglycerides. In addition, all molecules have positive relation with fasting glucose, fasting insulin and IR, being the ICAM-1 also related to postprandial glycemia.

Therefore, although there were significant progress in understanding the involvement of E-selectin, P-selectin, VCAM-1, ICAM-1 and the chemokine MCP-1/CCL2 in regulating subclinical inflammation, studies linking these CAMs to anthropometric markers, body composition, biochemical and dietary parameters in healthy and obese individuals are still needed to elucidate these associations and mechanisms, since these are contributing factors for cardiovascular events due to its inflammatory effects on vascular endothelium.

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Revisión

Glycemic index role on visceral obesity, subclinical inflammation and associated chronic diseases

Patricia Feliciano Pereira, Crislaine das Graças de Almeida and Rita de Cássia Gonçalves Alfenas

Universidade Federal de Viçosa. Brazil.

Abstract

Background: It is believed that the glycemic index (GI) may be used as a strategy to prevent and control non-communicable diseases (NCD). Obesity is a multifactorial condition, a risk factor for development of other NCDs. Among the different types, abdominal obesity is highlighted, which is essential for the diagnosis of metabolic syndrome, and it is related to insulin resistance, dyslipidemia, hypertension and changes in levels of inflammatory markers. Such indicators are closely related to the development of Type 2 Diabetes and cardiovascular disease.

Objectives: Discuss the role of GI as a strategy for the prevention and/or treatment of visceral obesity, subclinical inflammation and chronic diseases.

Results and discussion: The intake of low GI diets is associated with glycemic decreases, and lower and more consistent postprandial insulin release, avoiding the occurrence of hypoglycemia. Moreover, consumption of a low GI diet has been indicated as beneficial for reducing body weight, total body fat and visceral fat, levels of pro-inflammatory markers and the occurrence of dyslipidemia and hypertension. The intake of low GI foods should be encouraged in order to prevent and control non-communicable diseases.

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Key words: *Glycemic index. Obesity. Insulin resistance. Inflammation. Cardiovascular diseases.*

PAPEL DEL ÍNDICE GLUCÉMICO EN LA OBESIDAD VISCERAL, INFLAMACIÓN SUBCLÍNICA Y LAS ENFERMEDADES CRÓNICAS

Resumen

Introducción: Se cree que es posible emplear el índice glucémico (IG) como estrategia para prevenir y controlar enfermedades no-comunicables (ENC). La obesidad es un estado multifactorial, un factor de riesgo para el desarrollo de otras ENC. Entre las distintas manifestaciones de la obesidad, destaca la obesidad abdominal, que es fundamental para el diagnóstico del síndrome metabólico y está relacionada con resistencia a la insulina, dislipidemia, hipertensión y cambios en los niveles de marcadores inflamatorios. Estos indicadores están estrechamente relacionados con el desarrollo de diabetes de tipo 2, así como de enfermedad cardiovascular.

Objetivos: Debatir el papel del IG como estrategia para la prevención y/o tratamiento de obesidad visceral, inflamación subclínica y enfermedades crónicas.

Resultados y debate: La ingesta de dietas con bajo IG está asociada a incrementos glucémicos, así como una insulina postprandial más baja y más consistente, evitando la aparición de hipoglucemia. Además, el consumo de una dieta de bajo IG ha sido identificado como beneficioso para la reducción del peso corporal, la grasa corporal total y la grasa visceral, los niveles de marcadores pro-inflamatorios y la aparición de dislipidemia e hipertensión. Se debería fomentar la ingesta de alimentos con bajo IG para prevenir y controlar enfermedades no-comunicables.

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Palabras clave: *Índice glucémico. Obesidad. Resistencia a la insulina. Inflamación. Enfermedades cardiovasculares.*

Correspondence: Patricia Feliciano Pereira.
Universidade Federal de Viçosa.
Brazil.

E-mail: pfelicianopereira@gmail.com

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Abbreviations

BMI: Body mass index.
CD40L: Membrane glycoproteins expressed on the surface of T cells.
NCD: Non-communicable diseases.
FUNGENUT Study: Functional Genomics and Nutrition Study.
GI: Glycemic index.
GL: Glycemic load.
GPx: Glutathione peroxidase.
HDL: High density lipoprotein cholesterol.
ICAM-1: Intercellular adhesion molecule-1.
IL: Interleukin.
LDL: Low density lipoprotein cholesterol.
MCP-1: monocyte chemotactic protein-1.
MMP-9: Matrix metalloproteinase 9.
NADPH: Nicotinamide adeninedinucleotide phosphate.
ON: Nitric oxide.
PAI-1: Plasminogen activator inhibitor-1.
CRP: C-reactive protein.
MRP: Myeloid related protein.
US-CRP: Ultra-sensitive C-reactive protein.
TNF α : Tumor necrosis factor .
VCAM-1: Vascular cell adhesion molecule-1.

Introduction

Obesity is currently considered a global epidemic and results from changes in living standards and the environment in which humans live, leading to a gradual genotypic and phenotypic adaptation.¹ The number of overweight adults worldwide has surpassed 1.4 billion people, where 35% were considered overweight and 11% obese in 2008.² Reduced physical activity, the socioeconomic environment and consumption of energy-dense and palatable foods are probably the greatest contributors for establishment of this pattern.³

Many non-communicable diseases (NCD), the main causes of morbidity and mortality, have obesity as the common risk factor. NCDs related to obesity include ischemic heart disease, diabetes, stroke, cancer and hypertension.⁴

The consumption of hypolipidic diets has been widely used as a strategy for prevention and control of obesity.⁵ However, reduced fat intake is usually accompanied by increased consumption of foods with a high glycemic index (GI).⁶ It is believed that, in relation to the low GI, consumption of foods with high GI favors the occurrence of hyperglycemia and hyperinsulinemia, as well as hypoglycemia, which increases the feeling of hunger, thus hindering the successful treatment of obesity.⁷

On the other hand, consumption of a low GI diet has been associated with lower levels of pro-inflammatory markers such as plasminogen activator inhibitor-1 (PAI-1), C-reactive protein (CRP) and tumor necrosis factor α (TNF- α),^{8,9} as well as improved levels of serum total cholesterol and the LDL fraction.¹⁰ Several

studies have also presented the role of GI in adiposity, and thus in the occurrence of various diseases.¹¹⁻¹³

Despite the numerous scientific reports on the potential preventive and therapeutic effect of low GI diets for obesity control, no consensus has been reached on this subject. Accordingly, the objective of this review study was to critically investigate the role of GI as a strategy for prevention and/or treatment of visceral obesity, subclinical inflammation and chronic illnesses.

Methodology

The study was conducted using online databases (Web of Science, Science Direct, Pubmed and Scopus) with the following keywords: “glycemic index”, “glycemic load” and/or “obesity”, “visceral obesity”, “central obesity”, “body fat”, “body fat distribution” and “inflammation”. Papers were selected which related to population studies and clinical trials with humans or animals, published from 2003 to 2013, as well as other relevant studies published prior to these dates.

Carbohydrates, fibers and glycemic index

The GI was proposed by Jenkins et al.¹⁴ for classification of carbohydrates with regards to their physiological effects. This index is an indicator of the ability of the carbohydrate food source to increase postprandial glycemia. The GI is determined from the area below the glycemic response curve after consumption of a portion of the test food, containing 50 g or 25 g of available carbohydrates, expressed as a percentage of the same type of response obtained from the consumer for a standard food (normally glucose or white bread) by the same individual.¹⁵

In addition to the GI, the glycemic load (GL) is another parameter that has been used in studies to evaluate the impact of foods and meals on glycemia. The GL is obtained by multiplying the GI of the test food or meal, considering glucose as the standard food, with its available carbohydrate content.¹⁵ The result of this product should thus be divided by 100.¹⁶

The quantity and quality of carbohydrates may have an effect on cardiovascular risk factors. During the grain refinement process, there occurs the removal of original fibers, making these high GI foods. Intake of these foods results in rapid increase of glycemia and insulinemia, which may decrease satiety and increase the level of circulating free fatty acids.⁷ Acute hyperglycemia, along with other consequences, reduces the availability of nitric oxide and worsens endothelial vasodilation, with consequent increase in blood pressure, a precursor to cardiovascular diseases.¹⁷

The intake of dietary fiber may play a protective role against disorders associated with inflammation in obesity.^{18,19} However, the mechanisms involved in this process are not yet clear. In a study performed with adolescents, it was observed that dietary fiber intake was

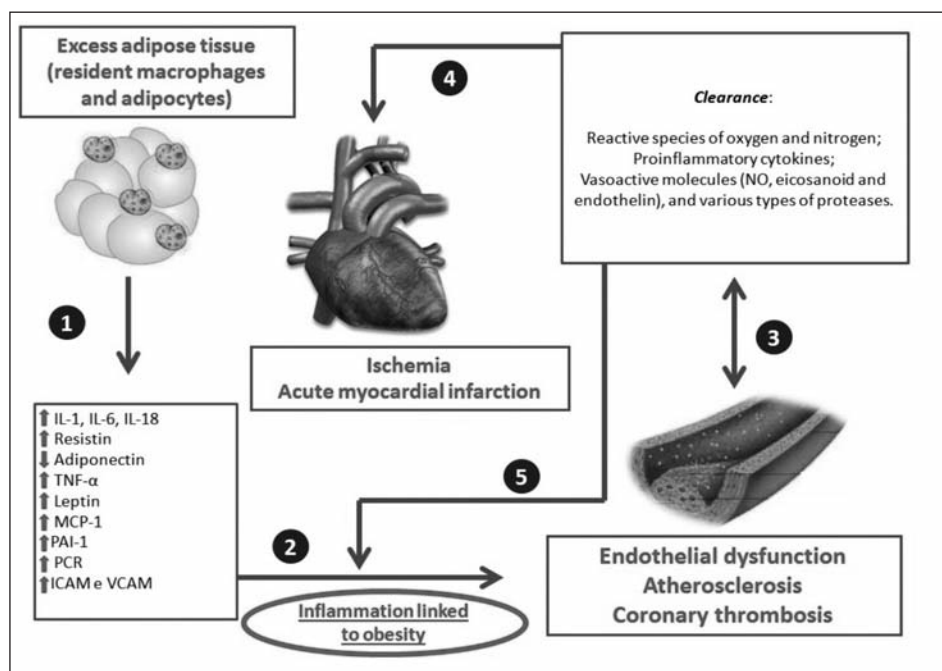


Fig. 1.—Possible mechanisms responsible for the association of visceral obesity versus inflammatory and atherothrombotic abnormalities. Legend: IL-1: interleukin 1, IL-6: interleukin 6, IL-18: interleukin 18; TNF-α: tumor necrosis factor α, MCP-1: monocyte chemoattractant protein-1; PAI-1: Plasminogen activator inhibitor-1; CRP: C-reactive protein; ICAM: intercellular adhesion molecule, VCAM: vascular cell adhesion molecule, NO: nitric oxide.

associated with lower visceral adiposity and improved inflammatory profile (CRP, leptin, fibrinogen and adiponectin).²⁰ The deposit of fat in the visceral region is closely related to subclinical inflammation. This type of low-grade inflammation plays a central role in the mechanisms that link obesity to cardiometabolic risk factors, and consequently, non-communicable diseases.^{21,22} It is interesting that the researchers evaluated the relationship between the fiber content consumed and GI of the tested meals, as well as insulinemia of the participating individuals, since it is suggested that the increased fiber intake has positive effects on insulin sensibility.¹⁹

Abdominal obesity, inflammation, endothelial dysfunction and atherosclerosis: general considerations

Central obesity, characterized by fat accumulation in the central region of the body, is a public health problem. The incidence of this type of obesity is higher than being overweight as diagnosed by the body mass index.²³ Central obesity is more strongly associated with metabolic changes that result from the deposition of fat in other regions.^{24,25}

Excess abdominal fat has recently been considered a *sine qua non*²⁶ for diagnosis of metabolic syndrome, which is associated with increased risk for cardiovascular disease.^{27,28} Accumulation of abdominal fat results in excessive liberation of fatty acids from the visceral adipose tissue, favoring the occurrence of hyperinsulinemia and insulin resistance, which are associated with an inflammatory and thrombogenic profile.^{21,22,29-31}

In this sense, obesity is considered a chronic systemic inflammatory disease,³² characterized by increased levels

of pro-inflammatory markers, such as adhesion molecules, including vascular adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1); cytokines such as tumor necrosis factor α (TNF-α) and interleukin 1, 6 and 18 (IL-1, IL-6 and IL-18); proteases such as matrix metalloproteinase 9 (MMP-9); platelet products such as CD40L and myeloid related proteins (MRP); acute phase proteins such as ultra-sensitive C-reactive protein (US-CRP), PAI-1; serum amyloid A and fibrinogen, and anti-inflammatory adipokines, such as adiponectin. Moreover, other clinical markers of inflammation have been reported, such as oxidized LDL and homocysteine.^{33,34}

Atherosclerosis results from chronic inflammation in response to interactions between plasma lipoproteins, cellular components including monocytes/ macrophages, T lymphocytes, endothelial cells, smooth muscle cells and the extracellular matrix of arteries.^{35,36}

Atherosclerotic lesions are considered inflammation producers, while high levels of CRP can induce atherosclerosis. Moreover, the release of inflammatory markers from visceral adipose tissue damages the vascular endothelium. The CRP appears to induce endothelial dysfunction, reduced nitric oxide production, hypertension and cardiovascular diseases³⁷ (fig. 1).

Role of the glycemic index on prevention and control of chronic diseases associated with obesity

Studies involving human subjects

Postprandial hyperglycemia is more strongly associated with increased release of free radicals and pro-inflammatory cytokines than fasting hyperglycemia.³⁸

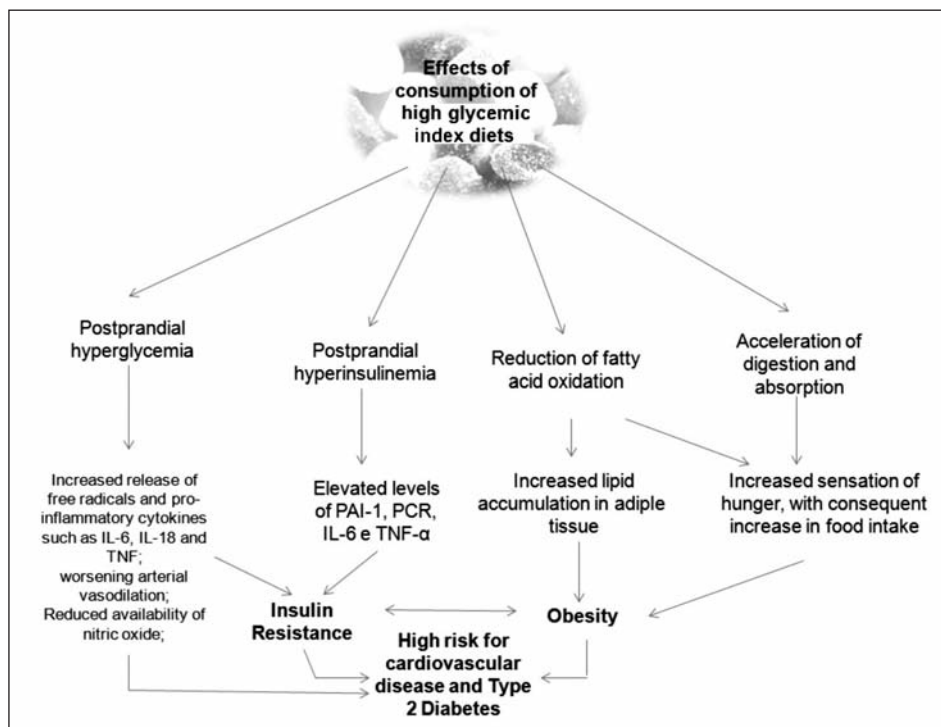


Fig. 2.—Main effects of the consumption of diets with high glycemic index on obesity, inflammation and associated diseases: Legend: IL-6: interleukin 6, IL-18: interleukin 18, TNF- α : tumor necrosis factor, PAI-1: plasminogen activator inhibitor-1, CRP: C-reactive protein.

The increased release of these factors is responsible for the deleterious effect of hyperglycemia on the vasculature²⁸ (fig. 2).

A cross analysis of the intake data from 780 diabetic men participating in the Health Professionals' Follow-Up Study indicated that consumption of low GL diets, independent of fiber content, may increase the serum concentrations of adiponectin, independent of the dose; this is an anti-inflammatory adipokine that, among other important effects on the metabolism, contributes to increased sensitivity to insulin.³⁹ In another study involving 511 elderly, higher levels of TNF- α and IL-6 were observed in the in the upper quartile of GI compared to the lower quartile in the baseline. After one year of monitoring, there was a decrease in levels of adiponectin and leptin in those who consumed diets with higher contents of GI and GL.⁴⁰ Leptin is a hormone produced by the adipose tissue, which controls food intake.⁴¹ Thus, results of the study performed by Bulló et al.⁴⁰ suggested that consumption of diets rich in GI and GL favor the occurrence of obesity and diabetes mellitus type 2.

In this context, in a study conducted among women with type 2 diabetes, it was found that consumption of whole grains and low GI reduced systemic inflammation.⁴² Thus, scientific evidence suggests that different carbohydrate types can modulate circulating levels of pro- and anti-inflammatory cytokines.

The typical western diet, rich in GI carbohydrates, including potatoes, bread and refined grains is rapidly digested and absorbed, resulting in increased insulin secretion.⁴³ Therefore, consumption of high GI foods by insulin-resistant individuals intensifies the increase

in postprandial glycemia and insulinemia, contributing to depletion of beta cells and development of type 2 diabetes⁴⁴ (fig. 2).

On the other hand, consumption of a low GI diet may maintain and/or improve insulin sensitivity, and also assist in weight loss.⁴⁵ Conversely, consumption of a low GI diet may help control obesity by promoting greater satiety⁴⁶ and increased fat oxidation,⁴⁷ resulting in reduction of total body fat^{3,48} and abdominal body fat, which is known to participate in development of chronic diseases.⁴⁹ These effects are summed with slower digestion and absorption with consequent effects on the reduction of postprandial glycemia and insulinemia.⁵⁰

In a study involving the participation of 933 Korean individuals, it was found that women who consumed a diet rich in GI and GL were more likely to be obese. On the other hand, a negative association was confirmed between the prevalence of obesity in men and consumption of the GL-rich diet.⁵¹ These results suggest that the mechanisms which contribute to prevalence of obesity may differ among genders.

Similarly, in another study involving Korean adults, it was reported that intake of diets rich in GI and GL increased the risk of women presenting hypertriglyceridemia and HDL-cholesterol lower than ideal. The risk of developing metabolic syndrome was increased among overweight women who consumed larger quantities of carbohydrates and diets rich in GI and GL. However, this increased risk was not observed among eutrophic women.²⁵ The results of this latest study suggest that body weight can modulate the effect of carbohydrate quantity and quality consumed on the manifestation of metabolic syndrome.

In a crossover study, overweight volunteers randomly participated in two stages (high GI or low GI), each lasting thirty consecutive days. During the study, volunteers ate two meals daily in the laboratory and an isocaloric portion of fruit outside the laboratory, with GI in accordance with the stage in which they participated. A significant reduction in measures of waist circumference and waist-hip ratio were observed after the low GI stage. However, no differences were observed in the BMI and total body fat.⁴⁹ These results reinforce that the consumption of low-GI diets may play an important role in reducing abdominal obesity and consequently chronic diseases, such as diabetes and cardiovascular diseases.

Similarly, in a prospective study with 48,631 men and women from five European countries, the influence of dietary factors on changes in abdominal adiposity was evaluated for an average period of 5.5 years. A significant increase in waist circumference was observed in both genders for a given BMI in those consuming the GI-rich diet with higher energy density. Among women, low fiber intake, increased GL and higher alcohol consumption were also predictors of increased abdominal adiposity.¹² Thus, the results suggest that consumption of the low-GI diet associated with low caloric intake may prevent visceral adiposity.

Similar results were observed in a 12 week study, in which women (BMI 25-45 kg/m²) who consumed a Mediterranean diet showed reductions in body weight, systolic blood pressure, triglyceride levels, total cholesterol and LDL-cholesterol.⁵² It should be noted, however, that study participants differed with regards to their level of adiposity, since participants included those considered overweight as well as morbidly obese. Thus, the variation in adiposity presented by study participants may have differently influenced the glycemic response and consequently the levels of the biochemical parameters evaluated.

Participants from Christchurch, New Zealand, were involved in dietary intervention programs via the internet, targeting the consumption of low GL diets. After 6 months, significant losses were observed regarding average weight (3.5 kg), along with reductions in BMI (1.2 kg/m²) and waist circumference (4.8 cm).⁵³ However, intake of a low GI diet for 18 months did not affect body weight of eutrophic Brazilian women between 25-45 years old.⁵⁴

The beneficial effects of consuming low GI/GL diets on obesity control have been reported by several authors.^{10,55} In one of these studies, the authors concluded that the low GI diet, offered for 5 weeks to overweight individuals, promoted greater weight loss than the high GI diet.⁵⁵ Similarly, consumption of a low GI diet by overweight or obese young adult women promoted greater weight and body fat losses when compared to the high GI diet.¹⁰ In obese adolescents, it was found that consumption of lower GL diets resulted in a greater reduction of BMI and body fat mass when compared to those consuming high GL diets.¹³

Regarding the lipid, glycemic and insulinemic profiles and inflammatory markers, results of the studies also show positive effects of the low-GI diet on total cholesterol and LDL cholesterol in humans.^{10,55} Furthermore, reductions in the LDL/HDL-cholesterol and total cholesterol/HDL-cholesterol ratios were reported, with no effect on insulin sensitivity in adult men and women.⁵⁵

However, in a cross-sectional population study with 668 non-diabetic subjects between 18 and 75 years old, no association was found between GI and insulin resistance.⁵⁶ Nevertheless, a positive effect was observed in an intervention study with obese children and adolescents, 7-13 years old, who consumed a low GI diet for 6 months.⁵⁷ It is believed that the beneficial effects of consuming the low GI diet were found only in the intervention study due to greater control of the nutritional composition of the diet consumed during the study.

Regarding the levels of inflammatory markers, the results of the studies are also conflicting. Consumption of the low GI diet by overweight women during 10 weeks reduced levels of the PAI-1 inhibitor, which participates in the regulation of angiogenesis and apoptosis.⁹ In a study with type 2 diabetics, consumption of two meals daily with high GI for 30 days resulted in higher levels of TNF- α when compared to the low GI diet.⁸ From the results of another study involving adult men and women with BMI of 27.4 ± 5.4 kg/m² and age of 48 ± 12 the existence of an inverse association was reported between GL and US-CRP levels among obese individuals.⁵⁸ Therefore, the results of recent studies^{8,9,58} suggest that consumption of high GI diets favor the installation of a profile of inflammatory markers capable of mediating installation of subclinical inflammation, which can promote the expression of NCD.

Studies involving animals

In relation to human studies, those involving laboratory animals have the advantage of providing information on the mechanisms and effects resulting from chronic consumption of low or high GI diets, as well as greater control over possible interfering factors.

In one of these crossover studies, the effect of ingesting diets with differing GI was assessed in adult rats for 32 weeks. Consumption of the GI-rich diet resulted in two times greater visceral fat, even after adjustment for total body fat. Contrarily, the subcutaneous adipose tissue did not differ between groups after adjustment for total fat. Lower levels of fat oxidation were observed in the high-GI group.⁵⁹

Furthermore, in C5BL/6 mice the effect of high or low GI diets was evaluated for 16 weeks, presenting high or low fat content. It was found that the postprandial glycemic response was greater in the high GI diet, independent of fat content. Although body weight did not differ between groups, mice fed a hypolipidic diet with high GL showed much higher adiposity than those fed a low-fat diet with low GI.¹¹

Glycemic index applicability

Insulin is a hormone involved in energy metabolism. Some of its various roles comprise enhancing glucose uptake and its utilization in the muscle and liver, increasing the hepatic conversion of glucose into glycogen, and inhibiting hormone-sensitive lipase leading to reduced release of fatty acids from adipose tissue, and thus presenting an anabolic function.⁴¹ The increase in serum insulin levels hinders weight loss⁵⁴ and is a predictor of the development of type 2 diabetes. Therefore, it is considered that the GI be used in nutritional interventions aimed at reducing body weight^{53,60,61} and improving the cardiometabolic profile.^{57,60}

The GI of specific foods can be obtained using international tables¹⁶ and websites (www.glycemicindex.com),⁶² which were created in order to avoid unnecessary repetition of tests for its determination. However, use of these values in research has its limitations, since many times these values may not accurately reflect the value displayed by a given type of food grown in different countries. The GI for a given food may vary in function of the preparation method of a food or meal, even if it presents the same nutrient composition.⁶³

However, estimated values of the GI obtained from the previously mentioned table and website^{16,62} can be used to estimate the GI, important tools for use in nutrition education.⁶⁴ The consumption of low GI foods has been recommended, especially among those who are already overweight and/or present glucose metabolism disorders.¹⁵

In countries like Australia, various commercialized foods present seals that facilitate the identification and preferential selection of low GI foods by the population (www.glycemicindex.com).⁶² The GI concept has been widely disseminated and used by the Australian population. This is a result of the efforts of researchers for practical application and for returning the results obtained in the laboratory to the population. Considering the expected overall increase in diabetes from 366 million in 2011 to 552 million in 2030,⁶⁵ the use of GI as a tool for nutrition education may be useful in weight control, cardiovascular risk and glycemic control.^{57,60,61}

Final considerations

The results of several studies suggest that the use of low GI foods favors the reduction of body weight, total and visceral adiposity, levels of pro-inflammatory markers, dyslipidemia and blood pressure. Thus, the GI should be considered an additional tool to be used for the selection of carbohydrate food sources, which should be included in a nutritionally balanced diet, able to promote and/or maintain proper health.

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Revisión

Effectiveness of inulin intake on indicators of chronic constipation; a meta-analysis of controlled randomized clinical trials

Luis Collado Yurrita¹, Ismael San Mauro Martín^{1,2}, María José Ciudad-Cabañas¹, María Elisa Calle-Purón³ and Marta Hernández Cabria⁴

¹Medicine's Department. Complutense University of Madrid. ²Research Centers in Nutrition and Health (CINUSA Group).

³Department of Preventive Medicine and Public Health. Complutense University of Madrid. ⁴Nutrition's Department. Corporación Alimentaria Peñasanta S. A. Spain.

Abstract

Background: Constipation is an intestinal dysfunction. Prebiotics, such as inulin, can improve bowel function by positively influencing intestinal biota.

Aim: To analyze the scientific evidence for the role of inulin in improving bowel function in patients with chronic constipation.

Methods: A meta-analysis of randomized controlled clinical trials was conducted, grounded on a literature search for the period 1995-2013 (descriptors: inulin & constipation) on PubMed, ScieLo and Central Trials Register Cochrane databases. A total of 24 articles were found, 5 of them were selected for this meta-analysis, involving 252 subjects (experimental group: n = 144, control group: n = 108). The quality of the studies was assessed using the Jadad scale.

Results: We found a significant overall effect of inulin on stool frequency (DEM = 0.69, 95% CI: 0.04, 1.34), stool consistency (Bristol scale) (DEM = 1.07, 95% CI: 0.70, 1.45), transit time (DEM = -0.57, 95% CI: -0.99, -0.15) and hardness of stool (RR = 0.42, 95% CI: 0.26, 0.70). Pain and bloating do not improve with inulin intake.

Conclusions: inulin intake has a positive effect on bowel function.

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Key words: Inulin. Constipation. Bowel function. Randomized controlled clinical trial. Meta-analysis.

EFICACIA DE LA INGESTA DE INULINA SOBRE LOS INDICADORES DEL ESTREÑIMIENTO CRÓNICO; UN META-ANÁLISIS DE ENSAYOS CLÍNICOS ALEATORIZADOS CONTROLADOS

Resumen

Introducción: El estreñimiento es una disfunción intestinal. Los prebióticos, como la inulina, pueden mejorar la función intestinal influyendo positivamente en la biota intestinal.

Objetivo: Analizar la evidencia científica del papel de la inulina en la mejora de la función intestinal en sujetos con estreñimiento crónico. **Materia y método:** se realizó un meta-análisis de ensayos clínicos aleatorizados controlados que fueron seleccionados en una búsqueda bibliográfica en el período 1995-2013 (descriptores: inulina & estreñimiento) en PubMed, ScieLo y el Registro Central de Ensayos Clínicos de Cochrane. Se encontraron 24 artículos, de los que 5 fueron seleccionados para este meta-análisis, que involucran a 252 sujetos (grupo experimental: n = 144; grupo control: n = 108). La calidad de los estudios fue evaluada con la escala Jadad.

Resultados: Se ha encontrado un efecto global significativo de la inulina sobre la frecuencia de las deposiciones (DEM = 0,69, IC 95%: 0,04; 1,34), la consistencia de las heces (Escala de Bristol) (DEM = 1,07, IC 95%: 0,70; 1,45), el tiempo de tránsito (DEM = -0,57, IC 95%: -0,99; -0,15) y la dureza de las heces (RR = 0,42, IC 95%: 0,26; 0,70). El dolor y la distensión abdominal no mejoran con la ingesta de inulina.

Conclusiones: La ingesta de inulina tiene un efecto positivo sobre la función intestinal.

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Palabras clave: Inulina. Estreñimiento. Función intestinal. Ensayo clínico aleatorizado. Meta-análisis.

Correspondence: Luis Collado Yurrita.
Medicine's Department. Complutense University of Madrid.
Plaza de Ramón y Cajal s/n.
28040 Madrid (Spain).
E-mail: lcollado@ucm.es

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Abbreviations

C: Cases.
Gr: Gram.
M: Mean.
ml: Milliliter.
NR: Not reported.
P: Placebo.
RCT: Randomized clinical trial.
RR: Relative risk.
SD: Standar Desviation.

Introduction

Constipation is a common dysfunction characterized by a large combination of symptoms, among which hardness of stool, an incomplete sensation of evacuation, abdominal pains, swelling and distension, are included.¹

In the clinical scope, constipation is established based on the diagnostic criteria Roma III,² being necessary the achievement of, at least, two of the following in more than 25% of the stool frequency: a) effort; b) hard or compact stool; c) incomplete sensation of evacuation; d) sensation of blockage or obstruction; e) manual manoeuvres for evacuation; or f) less than three stool frequency per week. The epidemiological studies show figures of prevalence of this disorder, with values oscillating between 4, 4%³ and 81%⁴ considering the population characteristics, although, the majority of studies indicate a prevalence around 15% on adult population in occident.^{5,6} This bowel dysfunction negatively influences the quality of life of the individuals affected^{7,8} and could be related to an increment in the risk of suffering colorectal cancer.^{9,10}

In the past decade, interest for prebiotics, which are defined as non-digestible substances (food fibre), has increased considerably, resulting beneficial for the health of the individual, as they stimulate the growth or the activity of a certain number of the bacteria in the colon.¹¹ Prebiotics are fermentable oligosaccharides which are specifically designed to change the compositions and the activity of the intestinal microbiota, such as bifidobacterium and lactobacillus,¹² whose presence has been related to a beneficial effect on the consistency and the pH of the faeces, as well as the stool frequency.^{13,14} The ingestion of food fibre, thus, presents itself as a non-pharmacological option for the treatment of constipation.

Inulin is a prebiotic substance which functions in the same way as food fibre. It is a polysaccharide present in roots, tubers and plant rhizomes of common usage (chicory, garlic, artichoke, etc.), which is made by molecular chains of fructan of type $\beta(2\leftarrow 1)$, causing significant changes in the compositions of the intestinal microflora and improving intestinal habits.¹⁵

Although the evidences seem to indicate towards a beneficial effect of inulin on intestinal habits of people who suffer from constipation, there are few clinical

trials that provide enough guaranties in this sense. The aim of this study is to undertake a meta-analysis from the randomized clinical trails (RCT) in which the effect of inulin ingestion is analysed through the bowel function of people suffering from constipation.

Material and methods

Criteria of inclusion

The clinical trails which have been sellected are randomized studies which include one or more independent control groups and, one experimental group to which a food substance containing inulin was administered. A placebo substance (maltodextrin, lactose, etc.) was applied to the control groups, as specified on table I. The resulting values are indicators of the bowel function related to constipation (stool frequency, consistency, transit time, abdominal pain and bloating).

Criteria of exclusion

Duplicated studies, revisions, observational studies, clinical cases and crossed randomized clinical trails, have been excluded.

Research strategies and data extraction

A bibliographical search has been made on the following data bases: *PubMed*, *Central Registry of randomized clinical trials from Cochrane* and *ScieLo*. The terms of the search have been “inulin & constipation” (“inulina & estreñimiento”). The research has been carried out independently by two reviewers, reaching a consensus on the search results. In cases of disagreement, the participation of a third reviewer has been requested. The dates of publication have been enclosed between 1995 and 2013. 29 results have been obtained, from which 5 have been selected for this meta-analysis (fig. 1).¹⁶⁻²⁰ The others have been rejected for being randomized controlled clinical trails,¹⁰ for lack of data in the results⁵ or for being crossed controlled clinical trails.⁴ A search and article selection diagram has been drawn (fig. 1). For data extraction, a data base has been created for the different selected RCT, in which the results of each case has been registered. Subsequently, the results have been put together and grouped by common variables in the different studies. The variables, which were only present in one study, have been excluded, selecting only that data found at least in two of the RCT.

Statistic analysis

Data analysis has been made using Epidat® 3.1. Software. The categorical variables were analysed using

Table I
Characteristics of the selected trials

<i>Trial</i>	<i>Cases C/P</i>	<i>Age (years) Range M; ± Sd</i>	<i>Gender M/F</i>	<i>Intervention</i>	<i>Placebo</i>	<i>Conclusions</i>
López-Román et al., 2008 ¹⁶	16/16	47 ± 15	4; 28	Semi-skimmed milk (1/2 litre/day), 2 g/100 ml inulin, 2 g/100 ml MRD, 20 days	Semi-skimmed milk with vitamins A y D, 20 days	Improvement of the situation of primary cronic constipation idiopathic following Roma II criterion
Pilipenko et al., 2009 ¹⁷	(20 x 3)/16	18-72; 43.78	8; 68	Group 1: 150 g enriched yogurt (1.21 g/100 g); Group 2: 300 g enriched yogurt (0.31 g/100 g); Group 3: 200 g kefir (4 g/100 g). 14 days	Standere diet with an increment of diatetic food fiber (vegetables and dried fruit), 14 days	The insertion of inulin improved the health indicators related with constipation
Linetzky et al., 2012 ¹⁸	28/32	18-65	Women	15 g/day inulin, 3 weeks	15 g/ day maltodextrin, 3 weeks	The effects on the clinical indicators of constipation are comparable to those of the maltodextrin group
Weber et al., 2013 ¹⁹	20/24	4-12	na	Mixture of food fiber (Stimulance, "Milupa"), 12.5% inulin; 3.8 g of dilute fiber in 200 ml of milkshake for children > 18 kg; 7.6 g on children > 18 kg, twice/day, 4 weeks	Same dosage of maltodextrin, 4 weeks	The mixture of food fiber increases stool freacuncy and hardness
Isakov et al.,	20/20	na	na	Enriched yogurt (1.23 g/100 g), 125 ml twice/day, 2 weeks	Standered yogurt, 125 ml twice/day, 2 weeks	Enriched yogurt reduces the time of bowel transit and increases stool consistency

Characteristics of the studies: Consecutively showing a sample of each study (cases/controls); age (shown on the age range, on average and/or standard deviation); distributions of the participant's gender; type of intervention: placebo characteristics; conclusions of the different studies.

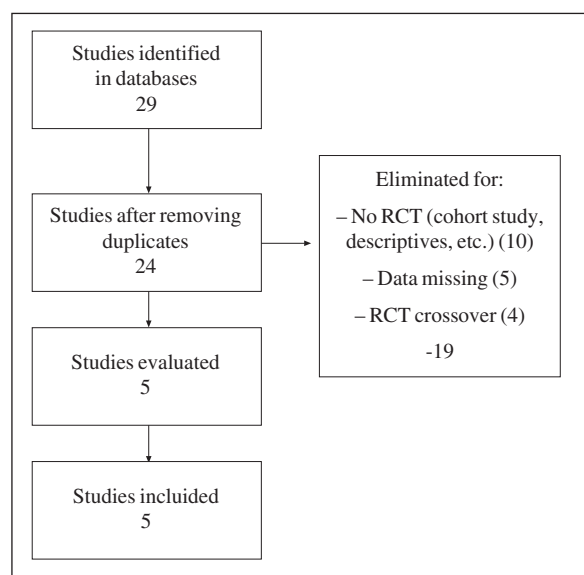


Fig. 1.—Diagram of selection of studies, representing how the studies were excluded and motives.

the relative risk (RR) procedure, while the constant variables have been analysed using the procedure of differentiation of standardized measures. A confidence interval of 95%, as well as the heterogeneity Dersimonian and Laird's Method has been calculated. When the result of the study was significant, the model of randomized effects was applied, employing the model of stable effects in the other cases. The publication bias was evaluated using Egger and Begg's test.

Results

Characteristics of the included studies

This study includes 5 articles which involve 252 subjects (144 in the experimental group and 108 in the control group). The general characteristics of this study, as well as those related to the interventions employed and the results of the trails can be found on table I.

Table II
Analysis of the quality of the trials by Jadad scale

Trial	Randomized	Randomization method	Doble-blind	Blinding	Withdrawal	Total
López-Román et al., 2008 ¹⁶	Yes	No	Yes	No	No	2
Pilipenko et al., 2009 ¹⁷	Yes	No	No	–	No	1
Linetzky et al., 2012 ¹⁸	Yes	No	Yes	No	Yes	3
Weber et al., 2013 ¹⁹	Yes	Yes	Yes	No	Yes	4
Isakov et al., 2013 ²⁰	Yes	No	No	No	No	1

Describes the qualify of the studies bases on the punctuation (0-5) of the Jadad scale, based on the various characteristics of the studies.

Analysis of the quality of the trials

The *Jadad Scale* has been applied for the evaluation of clinical trails, in which the following aspects have been evaluated: existence of randomization, description of the randomization method, adequacy of the method, doble-blind, description of the blinding technique, adequacy of the test and description of the faults of the study. The maximum punctuation is 5, indicating the highest quality of the study. On table II, it can be observed that none of the selected articles reach the highest punctuation. None of them describe the procedure of blinding and only the article of Weber et al.¹⁹ describes the randomization method.

Meta-analysis of the stool frequency

The five selected studies contain data to evaluate weekly stool frequency. The heterogeneity test has displayed a result statistically significant ($\chi^2_4 =$

21,92; $p = 0,000$), which suggests the use of the model of randomized effects. The global test of this model indicates a significant effect upon the administration of inulin in the weekly stool frequency (fig. 2). Nevertheless, an existing bias of publication has been found, as shown on *Egger's test* ($t_3 = 6,632$; $p = 0,007$). Also, the sensibility analysis (table III) shows lack of robustness on the meta-analysis results, due to the dependency laying on the results of all the studies included.

Meta-analysis of the consistency (Bristol Scale)

In this test, three studies have been included. The heterogeneity test does not allow to reject the invalid hypothesis of the homogeneity of the studies ($\chi^2_2 = 2,17$; $p = 0,338$), thus, the model of fixed effects has been applied. The global test of this model indicates a significant effect upon the administration of inulin in stool consistency according to

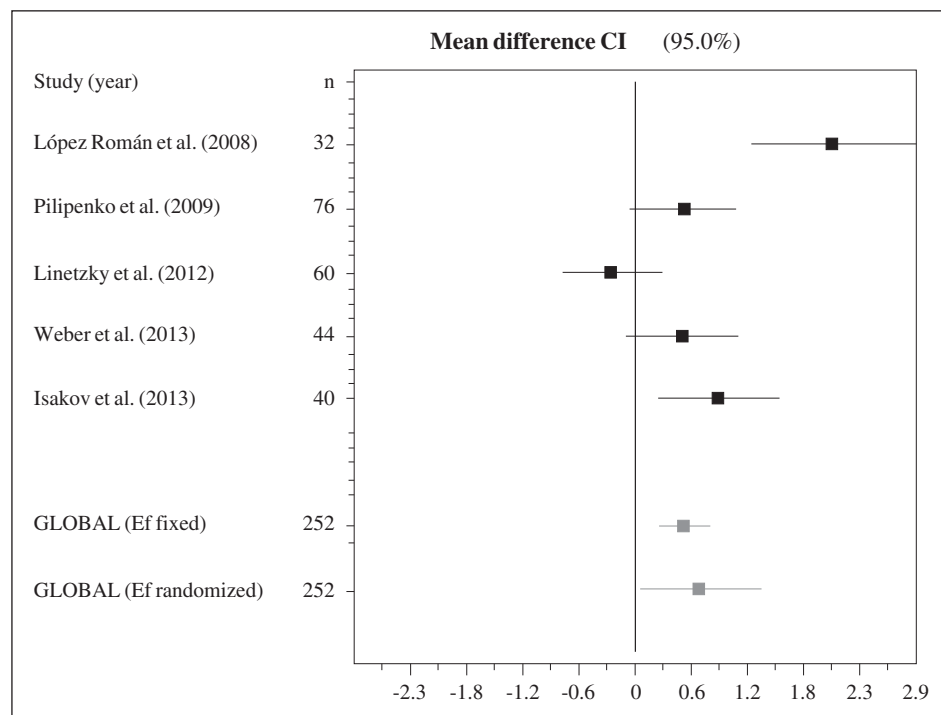


Fig. 2.—Graphic representation of the effects in the different trials and global estimation of the effects of the stool frequency meta-analysis.

Table III
Meta-analysis results: individual, global test and sensibility

Experimental group				Control group					
Stool frequency (weekly)									
Study	M	Sd	n	M	Sd	n	Weight %	DEM (IC 95%)	Sensibility
López-Román et al., 2008 ¹⁶	5.6	1.17	16	3.5	0.84	16	17.27	2.07 (1.21-2.93)	-43.87
Pilpenko et al., 2009 ¹⁷	5.39	2.18	60	4.27	2.1	16	20.95	0.52 (-0.04-1.08)	9.1
Linetzky et al., 2012 ¹⁸	5.95	2.5	28	6.7	3.83	32	21.5	-0.23 (-0.74-0.28)	33.92
Weber et al., 2013 ¹⁹	7.65	3.16	20	6.35	2.17	24	20.42	0.49 (-0.11-1.09)	9.84
Isakov et al., 2013 ²⁰	6.58	3.5	20	4.27	1.4	20	19.86	0.87 (0.22-1.51)	-4.71
Total			144			108		0.69 (0.04-1.34)	
Stool consistency (Bristol scale)									
Study	M	Sd	n	M	Sd	n	Weight %	DEM (IC 95%)	Sensibility
López-Román et al., 2008	4.53	0.85	16	3.28	1	16	41.25	1.24 (0.65;1.82))	-10.72
Pilpenko et al., 2009	3.67	0.9	60	2.62	0.6	16	34.74	0.69 (-0.05;1.33)	18.98
Isakov et al., 2013	3.1	1.3	20	2.4	0.6	20	24.01	1.35 (0.58-2.11)	-8.01
Total			96			52		1.07 (0.70-1.45)	
Transit time (minutes)									
Study	M	Sd	n	M	Sd	n	Weight %	DEM (IC 95%)	Sensibility
Pilpenko et al., 2009	115.57	25.83	60	132.8	41.9	16	56.98	-0.58 (-1.14;-0.02)	
Isakov et al., 2013	109	30.4	20	12.7	34.1	20	43.92	-0.56 (-1.19;0.07)	
Total			80			36		-0.57 (-0.99;-0.15)	
Abdominal pain									
Study	M	Sd	n	M	Sd	n	Weight %	DEM (IC 95%)	Sensibility
Pilpenko et al., 2009	1.32	0.53	60	1.25	0.4	16	51.82	0.14 (-0.41;0.69)	
Isakov et al., 2013	1.1	0.3	20	1.4	0.5	20	48.18	-0.73 (-1.37;-0.09)	
Total			80			36		-0.28 (-1.12;0.57)	
Abdominal distension									
Study	M	Sd	n	M	Sd	n	Weight %	DEM (IC 95%)	Sensibility
Pilpenko et al., 2009	1.53	0.73	60	1.8	0.6	16	55.75	-0.38 (-0.93;0.17)	
Isakov et al., 2013	1.8	0.9	20	1.6	0.5	20	44.25	0.27 (-0.35;0.90)	
Total			80			36		-0.09 (-0.51;0.32)	
Stool consistency (hardness)									
Study	n	%	n	%	Weight %	RR (IC 95%)			
Pilpenko et al., 2009	20	40	24	83.3	21.78	0.27 (0.09;0.80)			
Isakov et al., 2013	16	21.4	16	71.4	78.22	0.48 (0.27;0.85)			
Total	36		40			-0.42 (0.26;0.70)			

Join data of all the analysis – Stool consistency (hardness), abdominal distension, stool consistency (Bristol scale), transit time (in minutes), abdominal pain, stool frequency (weekly) – for the experimental group and control group, expressed in each of the cases in average, standard deviation, number of samples; the % of the weight of each study in the meta-analysis; and the standardized difference of the averages. In those cases where more than two studies were able to be included, sensibility has been included.

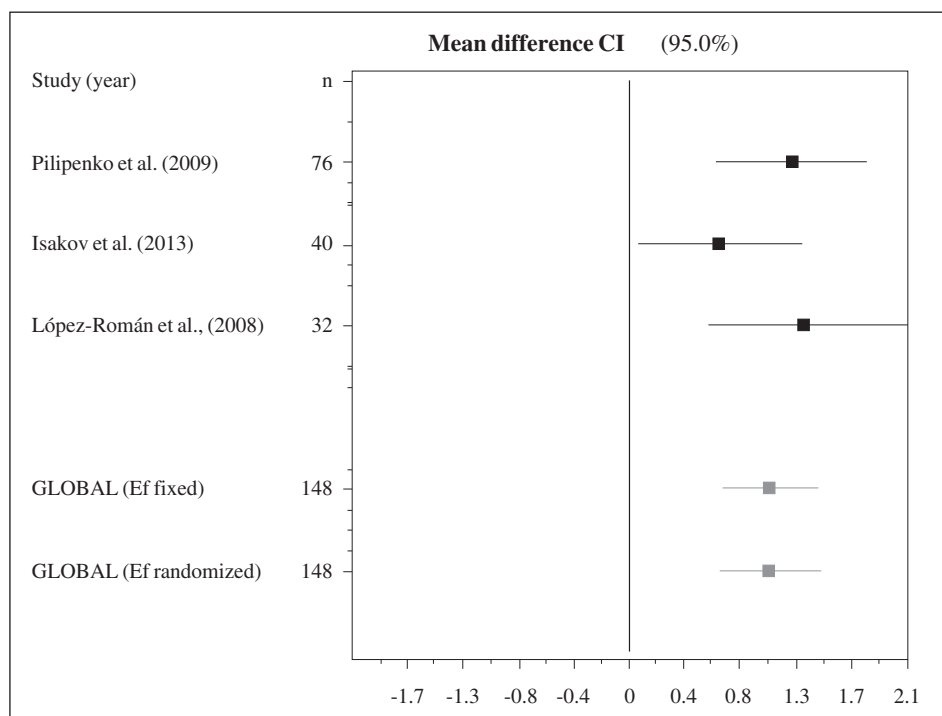


Fig. 3.—Graphic representation of the effects in the different trials and global estimation of the meta-analysis effect of stool consistency (Bristol scale).

Bristol Scale (fig. 3). The Egger test value ($t_1 = 0,252$; $p = 0,843$) allows to dismiss the presence of a publication bias. Nonetheless, the sensibility analysis (table III) points out an anomaly related to the robustness of the meta-analysis results, due to the variability of the global result dependent of each study included.

Consistency's meta-analysis (hardness)

In this meta-analysis, 2 studies have been included. The model of fixed effects has been applied due to the non-signification of the test to study the heterogeneity of the studies included ($\chi^2_1 = 0,84$; $p = 0,361$). The global test confirms the existence of a significant effect in the administration of inulin upon stool consistency-hardness (fig. 4). The value of Begg test ($z = 0,00$; $p = 1,000$) indicates absence of a publication bias. A sensibility analysis has not been developed because only two studies were included.

Meta-analysis of transit time

For the meta-analysis of transit time (in minutes), two studies have been used. According to the heterogeneity test, the application of the model of fixed effects ($\chi^2_1 = 0,00$; $p = 0,961$) is adequate, advising the use of the model of fixed effects. The global test of this model shows a significant effect of the administration of inulin in the reduction of transit time (fig. 5). The Begg test value ($z = 0,00$; $p = 1,000$) allows to dismiss the presence of a publication bias. A sensibility analysis has not been developed because only two studies were included.

Meta-analysis of abdominal pain

In this case, two studies have been included. The heterogeneity test indicates that the model which should be applied is that of randomized effects ($\chi^2_1 = 4,03$; $p = 0,045$), advising the use of the model of fixed effects. According to the global test of this model, a significant effect of the administration of inulin in the reduction of abdominal pain does not exist (fig. 6). The Begg test value ($z = 0,00$; $p = 1,000$) indicates the absence of a publication bias. A sensibility analysis has not been developed because only two studies were included.

Meta-analysis of abdominal distension

Once again, Pilipenko et al.¹⁷ and Isakov et al.¹⁸ studies have been included. The model of fixed effects has been applied due to the non-signification of the test to study the heterogeneity of the studies included ($\chi^2_1 = 2,39$; $p = 0,122$). The global test does not allow the affirmation of the existence of a significant effect in the administration of inulin in the reduction of abdominal distension (fig. 7). The Begg test value ($z = 0,00$; $p = 1,000$) indicates the absence of a publication bias. A sensibility analysis has not been developed because only two studies were included.

Discussion and conclusions

The results obtained in the meta-analysis show that the administration of inulin produces a significant bene-

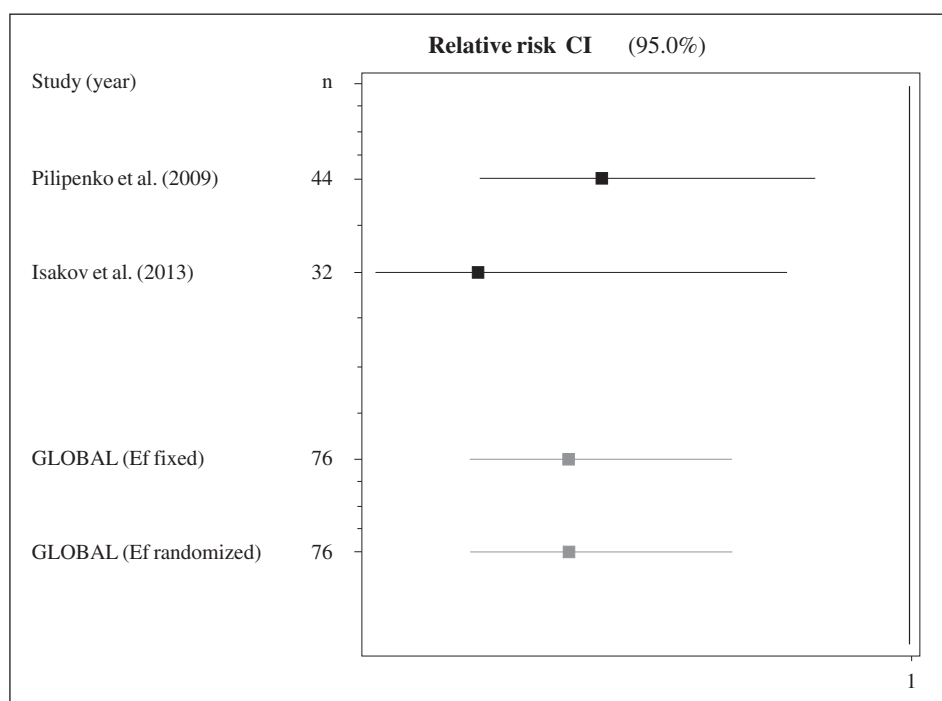


Fig. 4.—Graphic representation of the effects in the different trials and global estimation of the meta-analysis effect of the stool consistency (hardness).

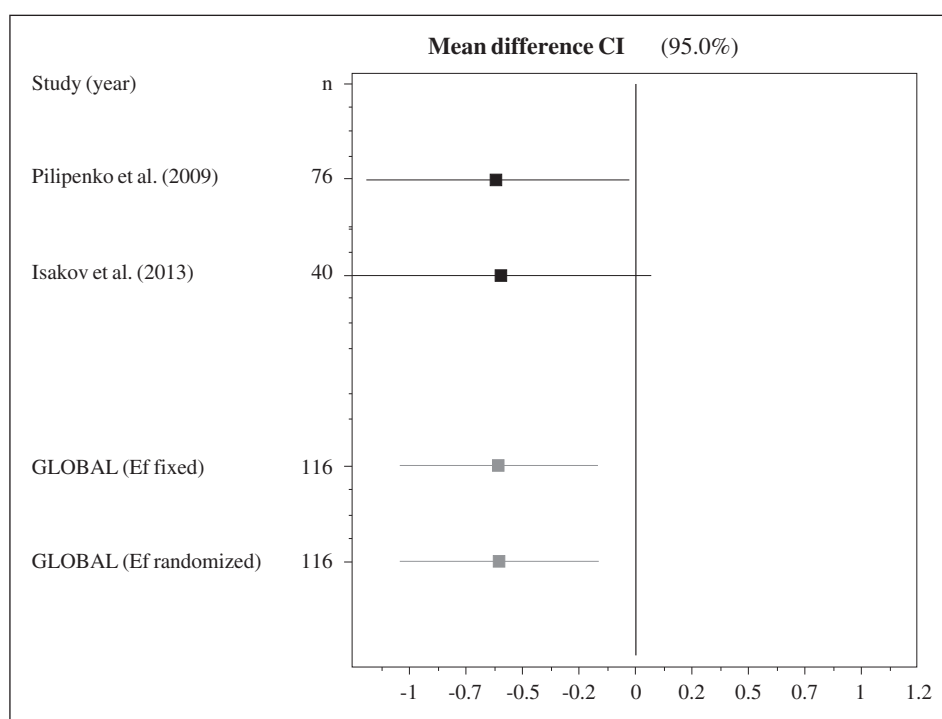


Fig. 5.—Graphic representation of the effects in the different trials and global estimation of the meta-analysis effect of transit time.

ficial effect upon various indicators of the intestinal function of evacuation in individuals with chronic constipation. An increase in the number of weekly stool frequency, a higher stool consistency according to the Bristol Scale, a lower intestinal transit time, as well as a reduction on the stool consistency has been observed. This demonstrates the beneficial effects of the ingestion of inulin for patients who suffer from chronic constipa-

tion in indicators that constitute essential aspects in this disorder. Nonetheless, the clinical trials examined have not produced a conclusive result in the reduction of abdominal pain and abdominal distension.

In relation to stool frequency, the results of this meta-analysis are in agreement with the ones observed in other studies.²¹⁻²⁵ Nevertheless, when evaluating the tolerance of inulin in one of the randomized crossed clinical trials

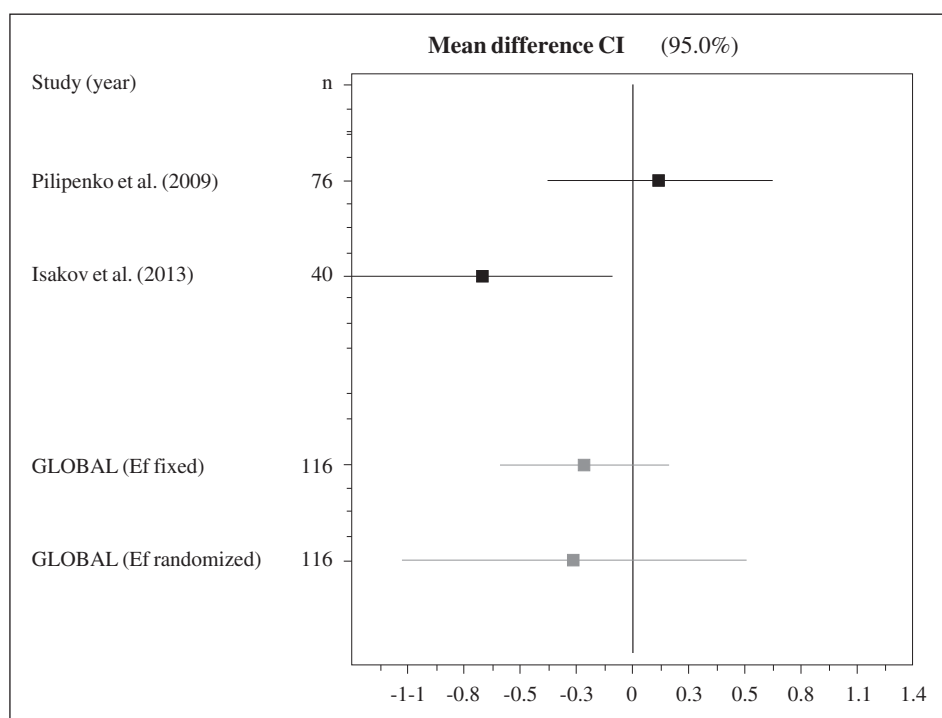


Fig. 6.—Graphic representation of the effects in the different trials and global estimation of the meta-analysis effects of abdominal pain.

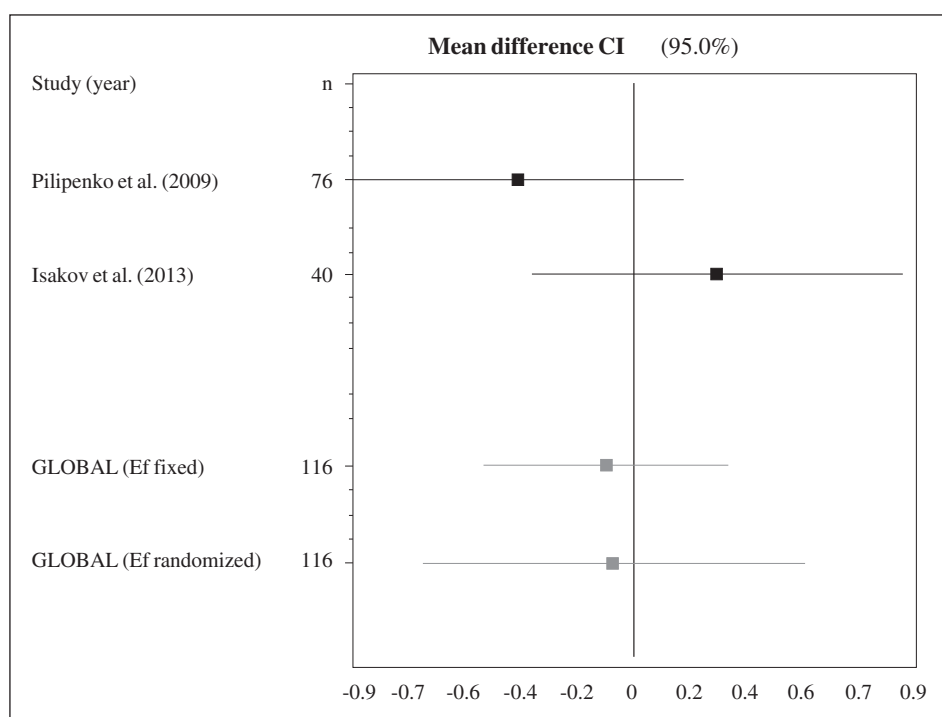


Fig. 7.—Graphic representation of the effects in the different trials and global estimation of the meta-analysis effects of abdominal distension.

made upon 84 patients, it was observed that stool frequency, although being a highly significant indicator of constipation, did not contribute decisively to the perception of the beneficial effects of the ingestion of this substance, as its most beneficial effects were indicated upon flatulence and stool consistency.²⁶

As far as the stool consistency according to Bristol Scale, our study confirms the findings of other clinical

trials which have not been included in this meta-analysis, for being crossed data that confirms the efficiency of inulin ingestion upon the increment of stool quality.^{21,25} One of the characteristics which better indicates stool quality is consistency, and in individuals with constipation, it presents itself hard, complicating evacuation. The ingestion of inulin has been associated, in our study, with a reduction of hardness in stool

frequency, which is in accordance with what was found in other studies,^{22,24,25} although there are other studies that have not found significant differences in the hardness of stool between the groups that were administered inulin and the placebo.^{21,23}

Another positive effect for the individuals with constipation, related to the ingestion of inulin, is the reduction of intestinal transit time, in accordance with the findings of other authors,²¹ for which the mechanisms associated with a higher speed in intestinal transit could be related to an increase in the peristaltic contractions, a reduction in anti-peristaltic contractions or a reduction of the contractions of the left colon. Other factors associated, could be the volume increment of the stool because a reduced re-absorption or the increment of the quantity of endoluminal bacteria, which represents approximately 60% of faecal volume. Nonetheless, other studies seem not to have found a positive effect upon the speed of intestinal transit as a consequence of inulin ingestion.²³

In relation to pain symptoms and abdominal distension, our study has not been able to establish a positive effect in inulin ingestion, as opposed to what was found in other studies.^{21,22,25} Nevertheless, in another experimental study, it has not been established that inulin ingestion is associated with a reduction of pain and abdominal distension,²⁴ showing the existing variability in the results on these indicators of constipation.

Therefore, it can be affirmed that, considering the examined clinical trails, inulin ingestion produces a beneficial effect upon bowel function of individuals with constipation in the frequency, consistency, quality, and transit time. Moreover, the administration of this product has not been linked with relevant adverse effects for the health of the patients, being a substance which is well tolerated by the organism in recommended dosages.²⁶ However, we should continue the investigation of the effects of inulin in bowel function, as the results of this meta-analysis is based upon a reduced sample of randomized clinical trails, this reflects the lack of scientific production related to this subject. These circumstances reduce the robustness of the conclusions, which need to be supported by clinical trails that recruit a greater amount of patient samples.

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Original / Obesidad

Association between childhood obesity and oral hygiene status

Eduardo Gomes Ferraz¹, Luciana Rodrigues Silva², Viviane Almeida Sarmiento³, Elisângela de Jesus Campos⁴, Thaís Feitosa Leitão de Oliveira¹, Juliana Cunha Magalhães¹, Gardênia Matos Paraguassú¹ and Ney Boa-Sorte⁵

¹DDS, MSc, PhD. School of Dentistry. Federal University of Bahia. Department of Pediatric Gastroenterology and Hepatology of the Professor Edgard Santos Teaching Hospital. Federal University of Bahia. Salvador. Bahia. Brazil. ²MD, MSc, PhD. School of Medicine. Federal University of Bahia. Department of Pediatric Gastroenterology and Hepatology of the Professor Edgard Santos Teaching Hospital. Federal University of Bahia. Salvador. Bahia. Brazil. ³DDS, MSc, PhD. School of Dentistry. Federal University of Bahia. Department of Propedeutics and Integrated Clinic. Federal University of Bahia. Salvador. Bahia. Brazil. ⁴DDS, MSc, PhD. Institute of Health Sciences. Federal University of Bahia. Department of Pediatric Gastroenterology and Hepatology of the Professor Edgard Santos Teaching Hospital. Federal University of Bahia. Salvador. Bahia. Brazil. ⁵MD, MSc, PhD. School of Medicine. Federal University of Bahia. Department of Nutrology of the Professor Edgard Santos Teaching Hospital. Federal University of Bahia. Salvador. Bahia. Brazil.

Abstract

Objective: The purpose of this study was to evaluate the oral hygiene status in pediatric obese patients.

Methods: A cross-sectional study was conducted from 2011 to 2012, which evaluated 180 Brazilian pediatric patients, 6-14 years old, girls and boys, recruited according to two Body Mass Index (BMI) categories: obese and non-obese (healthy weight). For the evaluation the oral hygiene status, the study used Oral Hygiene Index (OHI) and Gingival Bleeding Index (GBI).

Results: According to the total sample, 5/60 obese (8.3%) and 57/120 non-obese (47.5%) had good OHI, while 23/60 obese (38.4%) and 3/120 non-obese (2.5%) were classified in a low level of OHI, with a significance between the groups ($p < 0.001$), even after sorting by age. According to the classification of GBI, 60/60 obese (100.0%) and 89/120 non-obese (74.2%) had GBI 1 (bleeding gingiva), and 0/60 obese and 31/120 non-obese (25.8%) were classified as GBI 0 (healthy gingiva), with a significance between the groups ($p < 0.001$), even after sorting by age.

Conclusions: This study indicated that OHI and GBI were significantly higher in the obese children group.

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DOI:10.3305/nh.2014.30.2.7476

Key words: Pediatric obesity. Body mass index. Oral hygiene. Children.

ASOCIACION ENTRE LA OBESIDAD INFANTIL Y EL ESTADO DE HIGIENE ORAL

Resumen

Objetivo: El propósito de este estudio fue evaluar el estado de higiene oral en pacientes pediátrica con obesidad.

Métodos: Un estudio transversal realizado en Brasil en el período 2011-2012, que evaluó 180 pacientes pediátricos de 6 a 14 años, niños y niñas, reclutados en el Índice de Masa Corporal (IMC) y separados en dos categorías: obesos y no obesos (peso saludable). Para evaluar el estado de la higiene oral, el estudio utilizó Índice de Higiene Oral (OHI) y índice de sangrado gingival (GBI).

Resultados: De acuerdo con la muestra total, 5/60 obesos (8,3%) y 57/120 no obesos (47,5%) tuvieron buena OHI, mientras que 23/60 obesos (38,4%) y 3/120 no obesos (2,5%) fueron clasificados en un nivel bajo de OHI, con una significación entre los grupos ($p < 0,001$), incluso después de la clasificación por edades. De acuerdo con la clasificación de GBI, 60/60 obesos (100,0%) y 89/120 no obesos (74,2%) tenían GBI 1 (gingiva sangrante), y 0/60 obesos y 31/120 no obesos (25,8%) fueron clasificados como GBI 0 (gingiva sana), con una significación entre los grupos ($p < 0,001$), incluso después de la clasificación por edades.

Conclusiones: Este estudio indicó que OHI y GBI fueron significativamente mayores en el grupo de niños obesos.

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Palabras clave: Obesidad pediátrica. Índice de masa corporal. Higiene bucal. Niños.

Correspondence: Eduardo Gomes Ferraz.
Centro Pediátrico Professor Hosannah de Oliveira.
Serviço de Gastroenterologia e Hepatologia Pediátricas.
Rua Padre Feijó, s/n.
CEP: 40110-170 Canela. Salvador. Bahia. Brazil.
E-mail: ed_ferraz@yahoo.com.br

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Abbreviations

BMI: Body Mass Index.
OHI: Oral Hygiene Index.
GBI: Gingival Bleeding Index.
WHO: World Health Organization.
FOUFBA: Faculty of Dentistry, Federal University of Bahia.
HUPES: Pediatric Gastroenterology Unit of the Complex.
CPPHO: Pediatric Gastroenterology and Clinic of Obesity services.
DMFT: Number of decayed, missing and filled teeth.
TM: Trademark.
SPSS: Statistical Package for the Social Sciences.
CAPES: Coordination of Improvement of Higher Education Personnel.

Introduction

Obesity is characterized as a condition in which a person has excessive body fat, whose origin is associated to genetic and environmental factors.¹⁻⁴ Obesity is now considered by the World Health Organization (WHO) as a global epidemic.⁵ Obesity represents one of the most serious public health problems, both in childhood and in adulthood.⁶⁻⁸ Moreover, obese children often become obese adults and with serious health risks in the short and long term.⁹⁻¹¹

Considered a multifactorial disease, obesity causes limitations to the quality of life and is associated with several early and late complications, such as, cardiovascular, endocrine, metabolic, respiratory, liver disorders, and psychological and social disorders, as well as oral diseases, such as dental caries and gingival tissue changes.^{12,13}

Studies have reported an association between gingivitis and periodontitis in obese adults.¹⁴ As the main etiological factor for both diseases is represented by the accumulation of dental plaque, gingivitis is often observed in pediatric patients, whereas the diagnosis of periodontitis is less frequent in this group.^{15,16}

Some studies have evaluated this association in adolescents. Mod  er et al.¹⁷ when evaluating 65 obese and 65 non-obese patients of both genders, 10-18 years old, observed that 17 obese and 5 non-obese showed higher visible plaque index than the others, with a significant difference between the groups ($p = 0.005$). The presence of bleeding gingiva on probing was identified in 21 obese and 5 non-obese, with a significant difference between the groups ($p < 0.001$). According to the authors, the hyperinflammation of the periodontal tissue of obese is more prevalent than compared to non-obese, and in obese this is exacerbated by the presence of proinflammatory cytokines.

Regarding the studies of Fadel et al.¹⁸ based on the evaluation of clinical, microbiological and inflammatory parameters as indicators for caries and periodontal

disease in adolescents with obesity ($n = 27$) compared to 28 controls patients, 13-18 years old, the results showed that individuals with obesity had significantly more decayed tooth surfaces and gingival bleeding than controls even after controlling for confounders. The authors are unable to confirm whether differences in caries and gingival inflammation are due to systemic changes that are associated with obesity or due to possible irregular dietary/oral hygiene habits.

Besides the susceptibility to systemic diseases, obese individuals usually consume large amounts of caloric food containing saturated fat and low nutritional values, which could contribute to a poor oral health¹⁹. Thus, this study was designed to evaluate the oral hygiene status in pediatric obese patients.

Methods

Study design and sample

This was a cross-sectional study, approved by the Ethics Committee of the Faculty of Dentistry, Federal University of Bahia (FOUFBA) under registration (process CAAE 0014.0.368.000-10, FR 343856). The study was designed as an observational comparative survey of oral hygiene status in obese children versus non-obese ones. Statistical power was calculated using means and variances obtained from a previous pilot study. Calculation revealed that the recruitment of 180 subjects ensured a power more than 95% with a 95% confidence interval. The data collection occurred in the period from March 2011 to June 2012, in Salvador, Bahia, Brazil. From a total of 180 patients, 60 obese followed at the Pediatric Gastroenterology Unit of the Complex HUPES-CPPHO (UFBA), and 120 non-obese (healthy weight) followed at the FOUFBA; both genders, ages 6-14 years were selected. Subjects affected by pathologies or major medical conditions such as diabetes, or any kind of diagnosed immunological syndrome or those who consumed medications that could increase gingival volumes were not included in the study. The parents of the patients signed an informed consent form. For diagnosis of obesity, the subjects were weighed in light clothing using an electronic scale (W 200/5-WelmyTM) situation on a flat surface with a capacity of up to 200 kilograms, and their height was measured using a stadiometer to the nearest 5 millimeters. From these data, BMI was calculated using the Quetelet's equation (ratio of weight in kilograms by the square of height in meters). The result of the calculation was compared with the reference chart, according to WHO, in determining BMI percentile for children, both male and female.²⁰ Thus, patients were recruited into 2 groups: non-obese, for those in BMI percentile at or below the 85th percentile, and obese, for those in BMI percentile at or above the 97th percentile.²⁰ The patients with a BMI percentile between the 85th and 95th considered overweight were excluded. The parents of the

patients completed a questionnaire created for this study with questions about the eating habits, care of oral hygiene such as flossing and frequency of daily tooth-brushing. Soon after calculation of BMI, the individuals selected underwent clinical examination.

Oral examinations

The clinical examination was performed by a single researcher dentist, aided by an assistant, in an appropriate environment with a dental chair and artificial lighting. Initially, the evaluation of the presence of dental plaque and supragingival calculus was performed using the Oral Hygiene Index (OHI), according to Greene and Vermillion²¹ (1960), with air jets, a clinical mirror, and a WHO periodontal probe. The OHI is the combination of two components, the dental plaque index and the dental calculus index, which are estimated by 12 numerical determinations found in the labial and lingual/palatal surfaces of the teeth. The presence of dental plaque or dental calculus is examined in each sextant, using the tooth with the highest value for the calculation of the OHI. The value of the OHI (sum of the value of the dental plaque index and dental calculus index) can be classified as good (scores from 0 to 1.2), medium (scores 1.3 to 3), and low (scores of 3.1 to 6). After classifying OHI, we proceeded to Gingival Bleeding Index (GBI) to evaluate periodontal changes, such as the presence of gingival bleeding, with the aid of a WHO periodontal probe under the gingival sulcus of each permanent tooth present. The highest value score was recorded in the corresponding sextant to calculate the GBI. Thus, the result of the GBI for each patient was classified according to the following scores: code 0 (healthy gingiva), and code 1 (bleeding gingiva). Intra-examiner variability for OHI and GBI was assessed previously using a replicate examination of 10 young patients (aged between 10 and 14 years) and occurred 1 h after the first one. The researcher dentist was trained till reaching an intra-examiner calibration of more than 90% for both indexes. To exclude the effect of different status of dental permutation on plaque presence and gingival features, the indices were collected only from the first upper and lower molars and central and lateral incisors present in all subjects belonging to both groups. Sites on deciduous or newly erupted teeth were not considered in order to exclude the effect of exfoliation or immature status of the gingival complex on both plaque accumulation and inflammatory responses. During the clinical examination of the patients was also recorded the number of decayed, missing and filled teeth by the DMFT index.

Data analysis

All data were entered in EpidataTM and then transferred to Statistical Package for the Social Sciences,

version 13.0 (SPSS, Chicago, IL, USA) for statistical analysis. The Chi-square test was used for analysis of qualitative variables. In the comparison of means between two groups was used Student's t-test. Were considered significant the associations with error probability of 5% ($p < 0.05$).

Results

The study sample consisted of 180 patients distributed into two groups: 60 obese and 120 non-obese. The data distribution of the groups in relation to age and sex, as well as on oral hygiene and diet are shown in table I. Regarding the evaluation of oral hygiene, 19 OB (31.7%) and 62 UH (51.7%) underwent dental evaluation at least once a year, and 5 OB (8.3%) and 50 UH (41.7%) brushed their teeth three times a day. These variables showed significant differences between groups ($p < 0.001$). The practice of flossing was confirmed by only 2 OB (3.3%) and 23 UH (19.2%), demonstrating a significant difference between the groups ($p = 0.004$), as shown in table I.

According to table II, the OHI mean value of the sample of obese was 2.65, and 1.37 in non-obese, with a significant difference between the groups ($p < 0.001$), even after sorting by age. Regarding the OHI classification of the sample, only 5/60 obese (8.3%) and 57/120 non-obese (47.5%) showed good OHI, 23/60 obese (38.4%) and only 3/120 non-obese (2.5%) were classified in a low OHI, with a significant difference between the groups ($p < 0.001$), even after sorting by age, as shown in table II.

The distribution of the sample according to the GBI classification (table III) follows: 60/60 obese (100.0%) and 89/120 non-obese (74.2%) were GBI code 1 (bleeding gingiva), whereas 0/60 obese and 31/120 non-obese (25.8%) were classified in GBI code 0 (healthy gingiva), with a significant difference between the groups ($p < 0.001$), even after sorting by age, as shown in table III.

Regarding the DMFT index, 30 teeth (50.8%) in obese and 36 teeth (52.9%) in non-obese were decayed, 5 teeth (8.5%) in obese and 8 teeth (11.8%) in non-obese were missing, 24 teeth (40.7%) in obese and 24 teeth (35.3%) in non-obese were filled, without significant difference between groups ($p = 0.734$).

Discussion

Obesity and related diseases have in their dietary habits an important etiologic common component.^{2,22-24} In addition to physical inactivity and genetic factors, some studies have shown that many health conditions are affected by both obesity and, for those overweight during childhood, psychosocial disorders, cardiovascular diseases, hepatic steatosis, joint changes, and the persistence of obesity into adulthood.¹³

Table I
Absolute and relative frequency of the sample according to sociodemographic characteristics, oral hygiene and eating habits of the obese and non-obese paediatric patients in Salvador, Bahia, Brazil, 2012

Variables	Obese		Non-obese		Total		p
	n	%	n	%	n	%	
<i>Age</i>							
6-9 years	30	50.0	60	50.0	90	50.0	
10-14 years	30	50.0	60	50.0	90	50.0	
<i>Sex</i>							
Boys	30	50.0	60	50.0	90	50.0	
Girls	30	50.0	60	50.0	90	50.0	
<i>Frequency of dental evaluation</i>							
Not attending	34	56.7	32	26.7	66	36.7	< 0.001*
Once a year	19	31.7	62	51.7	81	45.0	
Twice a year	6	10.0	26	21.6	32	17.8	
Three times a year	1	1.6	0	0.0	1	0.5	
<i>Frequency of daily toothbrushing</i>							
Do not brush your teeth	1	1.7	0	0.0	1	0.6	< 0.001*
Once a day	18	30.0	8	6.7	26	14.4	
Twice a day	35	58.3	60	50.0	95	52.8	
Three times a day	5	8.3	50	41.7	55	30.6	
More of three times a day	1	1.7	2	1.6	3	1.6	
<i>Flossing</i>							
No	58	96.7	97	80.8	155	86.1	= 0.004*
Yes	2	3.3	23	19.2	25	13.9	
<i>Type of diet</i>							
Normal	30	50.0	98	81.7	128	71.1	< 0.001*
High-fat	12	20.0	5	4.2	17	9.4	
High-carbohydrate	16	26.7	17	14.1	33	18.4	
No answer	2	3.3	0	0.0	2	1.1	
<i>Consumption of sweets</i>							
Low	5	8.3	34	28.3	39	21.7	= 0.001*
Medium	32	53.3	68	56.7	100	55.6	
High	21	35.0	16	13.3	37	20.6	
Too high	2	3.4	2	1.7	4	2.1	
<i>Frequency of daily snacks</i>							
Once a day	0	0.0	6	5.0	6	3.3	< 0.001*
Twice a day	11	18.3	86	71.7	97	53.9	
Three times a day	40	66.7	27	22.5	67	37.2	
More of three times a day	9	15.0	1	0.8	10	5.6	
<i>Food consistency</i>							
Liquid	14	23.3	34	28.3	48	26.7	< 0.001*
Pasty	31	51.7	9	7.5	40	22.2	
Solid	15	25.0	77	64.2	92	51.1	

*Chi-square-test.

The diseases that most commonly affect the stomatognathic system, such as dental caries²⁵ and periodontal disease, are caused by specific microorganisms found in dental biofilm.²⁶ In this context, the regular removal of supra and subgingival plaque can be considered as the main factor for preventing and treating these diseases. Furthermore, removal of the supragingival plaque is associated with the prevention of gingivitis and periodontitis.²⁶

Although several authors reported an association between obesity and periodontal disease in adults,¹⁴ few studies highlight this association in children, since none of these studies included groups of exclusively

children or adolescents. Thus, there is always a considerable heterogeneity in the age group evaluated, making it difficult to conclude whether a true correlation between obesity and periodontal disease indeed exists within a specific juvenile age group.^{19,27}

In the present study, no difference was observed between the groups regarding the evaluation of the number of decayed teeth ($p = 0.734$), however the results in table III highlight a higher prevalence of gingivitis (GBI code 1) in obese patients, for both age groups. This result is consistent with reports from Franchini et al.¹⁶ which evaluated the prevalence of gingivitis associated with BMI in 98 patients (66

Table II
Distribution of the sample according to OHI evaluation of the obese and non-obese paediatric patients in Salvador, Bahia, Brazil, 2012

Variables	Obese		Non-obese		Total		p
<i>Sample</i>							
Dental plaque index, M ± SD	2.62 ± 2.28		1.36 ± 1.63		1.78 ± 1.85		<0.001*
Dental calculus index, M ± SD	0.03 ± 0.10		0.01 ± 0.03		0.02 ± 0.05		
OHI, M ± SD	2.65 ± 1.94		1.37 ± 1.36		1.80 ± 1.56		
<i>6-9 years</i>							
Dental plaque index, M ± SD	2.53 ± 2.34		1.51 ± 1.69		1.85 ± 1.91		<0.001*
Dental calculus index, M ± SD	0.02 ± 0.05		0.01 ± 0.02		0.01 ± 0.03		
OHI, M ± SD	2.55 ± 2.01		1.52 ± 1.43		1.86 ± 1.62		
<i>10-14 years</i>							
Dental plaque index, M ± SD	2.71 ± 2.21		1.21 ± 1.58		1.71 ± 1.79		<0.001*
Dental calculus index, M ± SD	0.05 ± 0.15		0.02 ± 0.05		0.03 ± 0.08		
OHI, M ± SD	2.76 ± 1.88		1.23 ± 1.30		1.74 ± 1.49		
<i>OHI classification (sample)</i>							
Good, n / %	5	8.3	57	47.5	62	34.4	<0.001**
Medium, n / %	32	53.3	60	50.0	92	51.1	
Low, n / %	23	38.4	3	2.5	26	14.5	
<i>OHI classification (6-9 years)</i>							
Good, n / %	0	0.0	25	41.7	25	27.8	<0.001**
Medium, n / %	23	76.7	32	53.3	55	61.1	
Low, n / %	7	23.3	3	5.0	10	11.1	
<i>OHI classification (10-14 years)</i>							
Good, n / %	5	16.7	32	53.3	37	41.1	<0.001**
Medium, n / %	9	30.0	28	46.7	37	41.1	
Low, n / %	16	53.3	0	0.0	16	17.8	

M, mean; SD, standard deviation.

*Student's t-test.

**Chi-square-test.

Table III
Distribution of the sample according to GBI evaluation of the obese and non-obese paediatric patients in Salvador, Bahia, Brazil, 2012

Variables	Obese		Non-obese		Total		p
	n	%	n	%	n	%	
<i>Sample</i>							
Code 0	0	0.0	31	25.8	31	17.2	< 0.001*
Code 1	60	100.0	89	74.2	149	82.8	
<i>6-9 years</i>							
Code 0	0	0.0	15	25.0	15	16.7	= 0.003*
Code 1	30	100.0	45	75.0	75	83.3	
<i>10-14 years</i>							
Code 0	0	0.0	16	26.7	16	17.8	= 0.002*
Code 1	30	100.0	44	73.3	74	82.2	

*Chi-square-test.

obese/overweight and 32 non-obese), both genders, 10-17 years old. The results showed that the gingival index was higher in obese/overweight (1.20) compared to non-obese (0.76), and the plaque index of the obese (1.42) compared to non-obese (0.77) was also higher. According to the authors, the main factor responsible for gingivitis is dental plaque accumulation. Furthermore, gingivitis observed in young patients with obesity is probably due to a combination of metabolic

disorders and inflammatory profiles, as a result of lack of care with oral hygiene procedures and information about diet.

The higher prevalence of gingivitis in obese in this study can be justified by the results of the interview regarding oral hygiene habits (table I), in which only 8.3% reported brushing their teeth three times a day, and only 3.3% reported flossing, which, as Rode et al.²⁶ characterized it, is one of the mechanical methods that is

among the most used preventive measures for the control of supragingival biofilm. Also, according to table I, 56.7% obese reported that they do not attend regular dental visits. Another important issue to note is that the obese appears to have lower overall healthcare assistance when compared to non-obese. This feature can also be reflected in their oral health and predisposition to increased risk of developing periodontal changes.¹⁶

A variety of potential mechanisms may explain the association between obesity and periodontal changes. Young overweight individuals may have unhealthy eating habits, such as inadequate intake of nutrients and excess sugar and fat, and such eating patterns can increase the risk for periodontal disease.²⁸ Moreover, alterations in host immunity or high levels of stress, which are often associated with excess fat gain in early life, may also play a role in developing disease.²⁹ Behaviors of low self-esteem and poor self-care in these patients, associated with social difficulties, also contribute to these results, as well as the probable influence of family behaviors.

The underlying biological mechanisms regarding the association of obesity with periodontitis are not well established. However, adipose tissue-derived cytokines and hormones may be one since the adipose tissue is not merely a reservoir of triglycerides, but also produces high levels of cytokines and hormones known as adipokines or adipocytokines, which in turn can affect periodontal tissues.³⁰

Obesity may also influence the state of the periodontal disease due to increased levels of lipids and glucose in the blood, which in turn can have deleterious consequences for the host response, including changes in the levels of T cells, monocytes, the function of the macrophages, and increased cytokine production.³⁰ Thus, according to the biological plausibility of the association between obesity and periodontitis, obese individuals could have greater chance of tissue destruction in the presence of a lesion such as with periodontal infection.¹⁶

Pediatric dentists should consider the relationship between body composition and oral health of patients, since they are the first professionals to do the diagnosis of oral abnormalities.³¹ It can be concluded in this study that the OHI and GBI were significantly higher in the obese children group, even after sorting by age. Moreover, we highlight the importance of teaching parents about the care needed with the oral hygiene for their children at this stage of life, especially in obese patients, who are more susceptible to gingival inflammation. All health professionals should have the knowledge to act in the prevention of obesity and prevention of diseases of the oral cavity, which are common in the currently.

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Original / *Obesidad*

Motivaciones y barreras de los niños chilenos; ¿amenazas u oportunidades para la implementación de las guías alimentarias 2013?

Sonia Olivares, Isabel Zacarías y Carmen Gloria González

Instituto de Nutrición y Tecnología de los Alimentos (INTA). Universidad de Chile. Chile.

Resumen

Introducción: La implementación de las nuevas Guías Alimentarias Basadas en Alimentos (GABA) para la población chilena, requiere el diseño de estrategias innovadoras y efectivas.

Objetivo: Determinar las motivaciones y barreras de niños y madres de preescolares ante los nuevos mensajes de las GABA, para identificar amenazas y oportunidades a considerar en el diseño de estrategias de comunicación e implementación aceptables para ellos.

Métodos: Estudio cualitativo, con 12 grupos focales de niños de 9 a 13 años y 6 grupos focales de madres de preescolares en el norte, centro y sur del país, para analizar su reacción ante cada uno de los 11 mensajes de las GABA 2013.

Resultados y discusión: Las respuestas de los niños y madres no mostraron diferencias por género (en el caso de los niños) o región del país. Se presentan los comentarios más frecuentes y representativos ante cada mensaje. Como amenazas para reducir el consumo de alimentos de alta densidad energética, altos en grasas, azúcares y sal se identificó la publicidad, gran oferta y bajos precios de este tipo de alimentos en las escuelas y en la calle. Las oportunidades identificadas incluyeron la publicidad de frutas, verduras y lácteos como facilitadoras de su consumo, así como la próxima implementación de la Ley 20.606, que se espera represente un apoyo efectivo a esta iniciativa.

Conclusión: Los resultados del presente estudio indican que el diseño de estrategias basadas en los valores, deseos y necesidades de los distintos grupos contribuirá a optimizar la implementación de las GABA en el país.

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Palabras clave: Guías alimentarias basadas en alimentos. Grupos focales niños. Motivaciones. Barreras.

MOTIVATIONS AND BARRIERS OF CHILEAN CHILDREN; THREATS OR OPPORTUNITIES FOR THE IMPLEMENTATION OF 2013 FOOD BASED DIETARY GUIDELINES?

Abstract

Introduction: Implementation of the updated Food Based Dietary Guidelines (FBDG) for the Chilean population requires the design of innovative strategies and effective.

Objective: To determine motivations and barriers for children and mothers of preschool-age children to follow new FBDG messages, aiming to identify challenges and opportunities for designing effective communication and implementation strategies.

Methods: A qualitative study based on 12 focus groups of 9 to 13 age children and 6 focus groups of mothers of preschool-age children, living in the north, central and south regions of the country, to analyze their reaction to each one of the 2013 FBDG messages.

Results and discussion: Answers of children and mothers did not show differences by gender (in the case of the children) or region of the country. Results show the most frequent and representative comments regarding each message. Challenges to reducing the consumption of foods high in energy, fat, sugar and salt include advertisements and plentiful supply and low prices for these types of foods, both in the school environment and on the street. Opportunities identified included the advertisement of fruits, vegetables and dairy products to promote their consumption, as well as the coming implementation of Law 20.606, which is expected to be an effective way to support this initiative.

Conclusion: The results of this study show that the design of strategies based on values, desires and needs of different groups will contribute to optimizing the implementation of the 2013 Chilean FBDG.

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Key words: Food based dietary guidelines. Children focus groups. Motivations. Barriers.

Correspondencia: Sonia Olivares.
Instituto de Nutrición y Tecnología de los Alimentos (INTA).
Universidad de Chile.
El Líbano 5524, Casilla 138. Correo 11.
Santiago, Chile.
E-mail: solivare@inta.uchile.cl / olivares.sonia@gmail.com

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Introducción

En la Conferencia Internacional sobre Nutrición (CIN) organizada por la Organización de las Naciones Unidas para la Agricultura y la Alimentación (FAO) y la Organización Mundial de la Salud (OMS), realizada en Roma el año 1992, se reconoció que las enfermedades crónicas no transmisibles (ENT) constituían un problema de salud pública que afectaba con mayor fuerza y gravedad a las poblaciones más vulnerables, lo que debía ser abordado por los países miembros a través de políticas públicas de carácter intersectorial. Esto dio origen a la recomendación de formular guías alimentarias basadas en alimentos (GABA), como una forma de educar a la población y orientarla en la selección de los más saludables¹. Posteriormente, en una reunión de expertos de la FAO y la OMS realizada en Chipre el año 1995, se establecieron las principales directrices para su elaboración, implementación y evaluación².

Chile publicó las primeras GABA el año 1997, en conjunto con el Ministerio de Salud, el Depto. de Nutrición y el Instituto de Nutrición y Tecnología de los Alimentos (INTA) de la Universidad de Chile³. El año 2005, el Ministerio de Salud publicó la segunda versión de las GABA como parte de la Guía para una Vida Saludable, que incluyó además recomendaciones sobre actividad física y aspectos psicosociales⁴.

El año 2012, el Ministerio de Salud adjudicó al INTA la licitación pública para la revisión y actualización de las guías alimentarias para la población chilena. En dicha licitación se explicitaba que, considerando el actual perfil epidemiológico de la población, caracterizado por una elevada y creciente tendencia al aumento en la prevalencia de sobrepeso, obesidad y otras ENT asociadas al sedentarismo y alto consumo de alimentos procesados de alta densidad energética y bebidas azucaradas en todos los grupos de edad⁵⁻⁷, las guías debían abordar la disminución del consumo de alimentos altos en calorías, grasas saturadas, azúcar y sal, además del aumento del consumo de frutas y verduras, lácteos, pescado, leguminosas y agua, incluidos en las guías anteriores^{3,4}.

Los Estados Unidos, uno de los países pioneros en la formulación de GABA, las que actualiza cada 5 años, en su versión del año 2010 muestra un énfasis en los mensajes referidos al balance energético, en los alimentos con alto contenido de grasas saturadas, azúcar y sodio que es necesario reducir, algunos alimentos de los que sería necesario aumentar el consumo en grupos específicos y en ayudar a su población a hacer elecciones saludables, entre las que destacan, además de la alimentación, la actividad física y las conductas para el control del peso^{8,9}.

En la revisión de las guías de 24 países realizada como parte de la formulación de las nuevas GABA para la población chilena¹⁰, se observó que si bien la mayoría de los países de América Latina las han publicado y varios las han actualizado, su difusión y en espe-

cial su implementación han sido insuficientes, por lo que no han tenido impacto en las tendencias alimentarias y en la disminución de la prevalencia de sobrepeso y obesidad. Esto fue ratificado en una reunión internacional realizada por la OPS/OMS con países de la Región¹¹ y en el estudio realizado por la FAO para determinar el estado de las Guías Alimentarias en América Latina y el Caribe 21 años después de la CIN¹².

Los estudios que han analizado el conocimiento e interpretación de los mensajes de las guías por la población chilena son escasos, y reflejan la falta de información y confusión existente, tanto sobre los mensajes, como en relación a los tamaños de las porciones de alimentos recomendadas^{13,14}.

La falta de campañas educativas que faciliten la comprensión de la población sobre la importancia de utilizar las GABA para prevenir el sobrepeso y la obesidad, no permiten esperar algún resultado sobre las conductas alimentarias, actualmente dominadas por el marketing de alimentos de alta densidad energética y bebidas azucaradas, que afectan con mayor fuerza a los niños y segmentos con menor nivel educacional, tanto a nivel nacional¹⁵ como mundial¹⁶.

La formulación de las GABA 2013 incluyó en una primera fase la formación de un Comité de Expertos del Ministerio de Salud, la FAO, universidades y encargados de programas de alimentación para distintos grupos de la población¹⁷. Este Comité elaboró una primera propuesta en la que definió 11 temas a abordar con las guías, de acuerdo a los solicitado por el MIN-SAL, a lo que agregó la información nutricional en las etiquetas de los alimentos envasados, obligatoria en el país desde el año 2006¹⁸.

Los expertos elaboraron 22 mensajes (2 por tema) que fueron sometidos a la aprobación y/o adaptación con 48 grupos focales (niños, adolescentes, adultos jóvenes y adultos mayores en distintas regiones del país). Los grupos eran de distinto género y nivel socio-económico (NSE medio alto y medio bajo)^{10,17}.

El objetivo de este estudio fue determinar las motivaciones y barreras de niños chilenos y madres de preescolares ante los mensajes de las nuevas Guías Alimentarias, con el fin de identificar amenazas u oportunidades a considerar en el diseño de estrategias de comunicación e implementación que resulten aceptables para ellos.

Métodos

Se trata de un estudio cualitativo en el que se realizaron 12 grupos focales con niños de 9 a 13 años y 6 grupos focales con madres de preescolares en tres regiones representativas del norte (Arica), centro (Santiago) y sur del país (Chillán-Concepción), para analizar su reacción ante cada uno de los 11 mensajes definitivos de las GABA 2013¹⁰.

En cada región se trabajó con 4 grupos de escolares: uno de niños y uno de niñas de NSE medio alto, uno de

Tabla I
Motivaciones y barreras de niños chilenos ante los mensajes relacionados con el balance energético y nutrientes críticos de las GABA 2013

1. *Para tener un peso saludable, come sano y realiza actividad física diariamente*
 - Si se hace ejercicio, se pueden eliminar las calorías y grasas extras del picoteo (“snacking”).
 - Cuando llego a mi casa abro el refrigerador y como cualquier cosa que me guste. En la noche como mejor porque mi mamá prepara la comida.
 - Los niños comen mucha chatarra, pero los adultos son los responsables de acostumbrarlos a comer con mucha azúcar y sal desde pequeños.
2. *Pasa menos tiempo frente al computador o la tele y camina a paso rápido, mínimo 30 minutos al día*
 - Con el computador podemos hacer de todo, estudiar y divertirnos al mismo tiempo.
 - Me cuesta dejarlo, hago todo por Internet, me conecto con mis amigos.
 - Es para los jóvenes porque son los que pasan más tiempo frente al computador y todavía pueden hacer cambios.
 - El mensaje es para todos porque es muy frecuente el uso de distintas pantallas.
3. *Come alimentos con poca sal y saca el salero de la mesa*
 - La sal disminuye la vida, por eso es bueno este mensaje, para no depender de la sal.
 - Cuesta seguirlo ya que está arraigado. La sal termina siendo una adicción.
 - Todo tiene sal, lo importante es no usar mucha. No es obligación echarle sal a todo.
 - Mi papá tiene hipertensión, así que en mi casa se come poca sal.
4. *Si quieres tener un peso saludable evita el azúcar, dulces, bebidas y jugos azucarados*
 - Es complicado porque hay mucha publicidad de cosas ricas, casi todas son dulces.
 - Los niños consumen muchas bebidas y comen azúcar desde pequeños, se acostumbran porque los papás premian con dulces.
 - Es difícil de cumplir, porque llevamos toda una vida comiendo azúcar.
 - Cuando a mi mamá le dijeron que tenía diabetes, yo dejé de comer azúcar.
5. *Cuida tu corazón evitando las frituras y alimentos con grasa, como cecinas (embutidos) y mayonesa*
 - Las cecinas (embutidos) siempre están en mi casa en la once y desayuno.
 - Me gustan mucho las papas fritas, no podría comerlas de otra manera.
 - Es difícil de realizar. El sabor de lo frito es más rico y las personas se acostumbran.
 - Es frecuente que toda la gente coma muchas cecinas (embutidos) y mayonesa.

niños y uno de niñas NSE medio bajo. En total se trabajó con 96 niños y niñas (32 por región). Se realizaron 2 grupos de madres de preescolares de distinto NSE en cada región.

Se clasificó como NSE medio bajo a los niños asistentes a escuelas públicas ubicadas en sectores de bajos ingresos y como NSE medio alto a los asistentes a colegios privados pagados, ubicados en sectores de altos ingresos, como se ha hecho en estudios previos¹⁵. Los grupos de madres fueron identificados en jardines infantiles privados (NSE medio alto) y de la Junta Nacional de Jardines Infantiles (NSE medio bajo).

En cada región, se invitó a los directores y profesores de una o dos escuelas públicas y colegios privados con gran número de alumnos de enseñanza básica y se solicitó la participación voluntaria de niños y niñas de 3° a 7° grados.

El estudio fue aprobado por el Comité de Ética del INTA, y contó con el consentimiento de los padres, directores y profesores. Los niños firmaron una carta de asentimiento, previa autorización de sus padres. Todas las madres fueron voluntarias que firmaron el consentimiento informado antes de participar.

En este estudio, la pregunta utilizada para abrir la discusión de los grupos focales ante cada mensaje fue

la siguiente: El mensaje que te presentamos ¿es fácil o difícil de realizar para ti? ¿Por qué? Las sesiones fueron grabadas y se realizó un análisis de contenido de las respuestas de cada grupo de participantes (niños o madres) según región, género y NSE. En las tres regiones, el nivel de saturación teórica¹⁹ se obtuvo al tercer grupo focal de niños. El cuarto grupo se realizó debido a que era necesario disponer de información comparable según región del país, género y NSE.

En los grupos focales, el tiempo de duración de las sesiones fue de 70 a 90 minutos.

Resultados

Debido a que las respuestas de los niños no presentaron diferencias por género o ciudad, se seleccionaron las más frecuentes y representativas ante cada mensaje. Se observó la misma semejanza en las respuestas de los grupos de madres, que son presentadas en una tabla separada. En las respuestas que mostraron diferencia según NSE esto es destacado en forma específica.

En la tabla I se incluyen las motivaciones y barreras más frecuentemente expresadas por los niños y niñas de las tres regiones sobre los mensajes relacionados

Tabla II*Motivaciones y barreras de niños chilenos ante los mensajes saludables de las GABA 2013***6. Come 5 veces verduras y frutas frescas de distintos colores cada día**

- Es fácil porque las frutas son dulces y a los niños les gustan las cosas dulces.
- En la mañana siempre como una fruta. La traigo al colegio de colación porque en el kiosco siempre hay pura comida chatarra.
- Este mensaje aparece en comerciales. Llama la atención, es entretenido.
- Es difícil de poner en práctica porque hay personas que no pueden comprar fruta todos los días (niños y niñas NSE medio bajo).

7. Para fortalecer tus huesos, consume lácteos bajos en grasa y azúcar 3 veces al día

- Es especial para los niños, porque fortalecen sus huesos. A los niños les gusta más tomar leche que a los adultos.
- Es más fácil cumplirlo hoy, porque hay mucha variedad de productos, por ejemplo los sin lactosa.
- Es sano realizarlo y se parece a los mensajes de la publicidad.
- Siempre tomo leche al desayuno y en el colegio. No me gusta la leche, la tomo por obligación. Prefiero el yogurt.

8. Para mantener sano tu corazón, come pescado al horno o a la plancha 2 veces por semana

- Ayuda más a los adultos comer pescado. También es bueno para los niños, pero a los que les gusta el pescado!
- Generalmente el pescado se come frito, da opciones para prepararlo distinto.
- Lo malo es que el pescado es más caro que la carne y no todos tienen acceso a él.
- Yo sé que los pescados enlatados traen sodio, entonces tampoco son buenos.

9. Consume legumbres al menos 2 veces por semana, sin mezclarlas con carne o cecinas

- Son ricas y es fácil consumirlas.
- Me gusta todo lo que sea legumbres. En mi casa siempre comemos. Mi mamá hace todos los lunes. En el colegio también nos dan.
- Comer porotos (frijoles) es más sano. Hay que evitar combinarlas con longanizas o tocino, sino igual hacen mal.
- Difícil de realizar porque son difíciles de preparar, hay que remojarlas desde el día anterior.

10. La mejor forma de mantenerte hidratado, es con 6 a 8 vasos de agua al día

- No cuesta nada tomar agua, sólo hay que hacerlo.
- Es bueno porque mucha gente toma bebida. El agua natural tiene mucho cloro, sería mejor agua embotellada.
- La bebida no calma la sed. Por eso el mensaje es bueno, porque cuando las personas tienen sed, toman bebidas y no agua.
- No hay hábito. Los deportistas son los que más la necesitan.

Tabla III*Motivaciones y barreras de niños chilenos ante el mensaje sobre etiquetado nutricional de las GABA 2013***11. Lee y compara las etiquetas de los alimentos y prefiere los bajos en grasas, azúcar y sal (sodio)**

- Es fácil seguir la indicación y da la alternativa de alimentos bajos en grasas y azúcar. Es necesario comparar el contenido de sodio, porque hace mal.
- Es para los adultos porque son los que compran. Los niños no hacen las compras de la casa.
- No entiendo para qué son las etiquetas. Mi mamá me enseña a fijarme en lo más importante, las calorías.
- No siempre es cierto lo que dicen las etiquetas.
- Es difícil de leer por el tamaño de la letra, muy pequeña. Es más importante el precio.

con el balance energético y los alimentos o nutrientes de los que sería necesario disminuir el consumo: sal, azúcar y grasas saturadas.

Las motivaciones y barreras más frecuentes de niños y niñas respecto a los mensajes sobre los alimentos saludables, de los que es necesario aumentar el consumo, se presentan en la tabla II.

En la tabla III se detallan las motivaciones y barreras respecto a la lectura de la información nutricional en las etiquetas de los alimentos envasados, especialmente relacionada con las guías referidas a los alimentos de alta densidad energética y elevado aporte de sodio, azúcar y grasas saturadas.

Las motivaciones y barreras de las madres de preescolares sobre las guías también se presentan en con-

junto para las 3 regiones. Cabe destacar que en general, la participación fue mayor en las madres de NSE medio bajo (tabla IV).

Discusión

Aunque la OMS, la FAO y el Instituto de Medicina de los Estados Unidos, entre otros, han señalado que existe evidencia científica convincente sobre los factores de riesgo cardiovascular asociados al sobrepeso, la obesidad, el sedentarismo y el alto consumo de grasas saturadas, azúcar y sal (sodio) y que han desarrollado estrategias para enfrentar la situación^{20,21}, al parecer la información difundida por los sistemas de salud y los

Tabla IV
Motivaciones y barreras de madres de preescolares chilenos ante los mensajes de las GABA 2013

<i>Mensajes GABA</i>	<i>Respuestas grupos focales madres</i>
1. Para tener un peso saludable, come sano y realiza AF diariamente.	- No se sabe qué es alimentarse adecuadamente, sólo lo que se ve y escucha en la tele. - Nos preocupamos más de las cosas materiales que de comer sano.
2. Pasa menos tiempo frente al computador o la tele y camina a paso rápido, mínimo 30 minutos al día.	- Cuesta dejar el computador, estamos siempre conectadas con las amigas y nos enteramos de cosas entretenidas. - Los niños pasan comiendo frente a la tele. Nadie se resiste frente a una pantalla. Se trabaja y se divierte uno con el computador. No me gusta caminar.
3. Come alimentos con poca sal y saca el salero de la mesa.	- Es más importante educar y acostumbrar a los niños. - En general el salero está en la mesa, es mejor decir que no añada más sal. Es muy impositivo.
4. Si quieres tener un peso saludable, evita el azúcar, dulces, bebidas y jugos azucarados.	- Cuesta dejarla, es como el motor del cuerpo. El comer dulce te activa a cualquier hora. - Es más fácil disminuir el azúcar que remplazarla. - Es mejor usar endulzante en vez de disminuir la cantidad de azúcar.
5. Cuida tu corazón evitando las frituras y alimentos con grasa, como cecinas y mayonesa.	- Mis hijos me reclaman porque no hago papas fritas. Y cuando comen las compran fuera. - En mi casa siempre tiene que haber mayonesa, trato de comprar light pero me reclaman.
6. Come 5 veces verduras y frutas frescas de distintos colores cada día.	- Para nosotros no hay problema porque siempre comemos bastante fruta y verdura. - Es mucha cantidad. Parece que fuera lo único que tenemos que comer. Que sean de diferentes colores es difícil.
7. Para fortalecer tus huesos, consume 3 veces en el día lácteos bajos en grasa y en azúcar.	- Te estimula y da opciones, hay más variedad. Es amable. - Los niños aceptan bien la leche y todos los lácteos. - La leche baja en grasa y azúcar es más cara (NSE medio bajo).
8. Para mantener sano tu corazón, come pescado al horno o a la plancha, 2 veces por semana.	- Sería positivo agregar que ayuda a reducir el colesterol - El pescado es caro y por eso no se come
9. Consume legumbres al menos dos veces por semana, sin mezclarlas con cecinas.	- Hoy en día están muy caras las legumbres, por lo que es más complicado consumirlas. - En mi casa no se consumen legumbres, a nadie le gustan. - No es fácil de lograr, es común agregarles carne o embutidos. Y demora más la preparación.
10. Para mantenerte hidratado, toma 6 a 8 vasos de agua al día.	- No puedo estar sin agua. Siempre ando con una botella. - Sé que es bueno, pero no consumo mucho. - Es difícil de llevar a cabo. Es más fácil tomar bebidas.
11. Lee y compara las etiquetas de los alimentos y prefiere los que tengan menos grasas, azúcar y sal (sodio).	- No sé comparar las etiquetas. Me fijo más en el precio. - Es poco realizable, - hace que sea muy demoroso comprar. - Sólo me fijo en la fecha de vencimiento, pero no comparo. - Compro lo que dice bajo en grasas.

medios no ha resultado suficiente para motivar conductas saludables en la población chilena, cuya prevalencia de obesidad y factores de riesgo cardiovascular son semejantes o superiores a los observados en países de mayor desarrollo^{5,6,8,22}.

En este estudio, se identificaron como amenazas para reducir el consumo de los alimentos altos en grasa,

azúcar y sal, el que los niños señalaran que sus fuentes de información eran la publicidad a través de la televisión, la gran oferta y bajos precios de estos alimentos en las escuelas y en la calle¹⁵. Si bien reconocieron los riesgos para la salud, ya que la existencia de familiares cercanos con diabetes o hipertensión fue otra fuente de información, señalaron que los mensajes orientados a

disminuir o evitar el consumo de estos productos estaban destinados a los adultos, a quienes responsabilizaron de acostumbrar a los niños a consumirlos en forma excesiva desde que eran pequeños.

Las madres también reconocieron la influencia de la publicidad sobre su consumo de este tipo de productos y destacaron lo difícil que les resultaba comer sano en sus hogares, por las preferencias y hábitos de la familia, en especial de los niños.

En este contexto, el rechazo al mensaje *“Pasa menos tiempo frente al computador o la tele y camina a paso rápido, mínimo 30 minutos al día”*, puede ser considerado otra amenaza, ya que tanto los grupos de niños como de madres, de ambos NSE, expresaron lo atractivo y frecuente que era el uso de estos medios en su vida diaria. Sólo algunas madres de NSE medio alto manifestaron realizar algún tipo de ejercicio 2 o 3 veces por semana.

Destacó en forma especial la resistencia ante el mensaje orientado a evitar el consumo de azúcares. Cabe señalar que la población chilena se encuentra entre la que consume mayor cantidad de bebidas azucaradas per cápita en el mundo^{7,23}. La evidencia científica reciente sobre la relación entre la alta ingesta de azúcares y los factores de riesgo cardiovascular en niños y adultos convierten a éste en uno de los problemas más preocupantes²⁴.

En un estudio realizado en Chile²⁵ con grupos focales de niños obesos de NSE medio bajo y sus madres, los niños mostraron una baja autoestima y deseaban bajar de peso, pero manifestaron que no contaban con el apoyo de sus padres. En efecto, sus madres señalaron *“la obesidad no se puede evitar”* y que *“no preparaban alimentos saludables porque a los niños no les gustaban y los adultos de la casa (incluyéndolos) preferían la comida “chatarra”*. En general, las intervenciones de educación en nutrición realizadas en las escuelas del país no incluyen a las madres, situación que ha sido observada en diversos estudios^{26, 27}.

En lo que respecta a los mensajes orientados a aumentar el consumo de alimentos saludables, los niños manifestaron que la publicidad de frutas, verduras y lácteos facilitaba su consumo, *“ya que ellos imitaban a los personajes de la publicidad”*. Esto significa que la publicidad podría convertirse en una oportunidad, si además de los alimentos citados, incorporara mensajes que motiven a los niños a disminuir el consumo de los que son menos saludables.

A diferencia de lo encontrado por O’Dea²⁸ al estudiar los beneficios y barreras ante la alimentación saludable y la actividad física en niños norteamericanos, quienes las relacionaron a un mejor rendimiento escolar, mayor autoestima, sentirse bien o divertirse con amigos, los niños chilenos sólo coincidieron con las barreras del citado estudio, destacando la mayor disponibilidad y mejor sabor de los alimentos menos saludables y la falta de control de los padres y la escuela sobre su consumo.

En este contexto, superar las barreras para la implementación de las GABA requiere de estrategias que ade-

más de informar adecuadamente a la población, logren crear un ambiente que facilite la adquisición de conductas saludables. El modelo ecológico social, planteado por los Estados Unidos para la implementación de sus GABA del año 2010⁹, considera la influencia de factores personales y ambientales sobre las conductas de las personas²⁹. Esto incluye la influencia del hogar, las escuelas y el entorno, planteando la necesidad de apoyo político para establecer regulaciones a la producción y publicidad de alimentos de alta densidad energética.

El año 2012, el Gobierno de Chile publicó la Ley 20.606 “Composición Nutricional de los Alimentos y su Publicidad”³⁰, que incluye la prohibición de vender alimentos de alta densidad energética en los establecimientos educacionales, y establece que los alimentos y bebidas que superen la cantidad de calorías, grasas saturadas, azúcar y sodio por porción establecida en dicha Ley, incluyan un mensaje de advertencia en sus envases. Las modificaciones al Reglamento Sanitario de los Alimentos para establecer esta regulación, aún en revisión, se espera que signifiquen una oportunidad para el diseño de campañas comunicacionales en los distintos organismos interesados en prevenir las ENT, de elevado costo para las personas, sus familias y toda la sociedad chilena.

Dado que el país no cuenta con una estrategia para la implementación de las GABA y su difusión se ha realizado principalmente a través de materiales educativos y algunas actividades en escuelas, el diseño de campañas de marketing social³¹ para la implementación con cada uno de los mensajes de las GABA, podría representar una gran oportunidad, ya que esta estrategia se basa en un completo diagnóstico de los valores, deseos, motivaciones y barreras de los distintos segmentos de la población, y mide su efectividad a través del logro de cambios de conducta en cada grupo objetivo.

Un modelo que ha avanzado varias etapas en esta dirección en el país es el Programa 5 al Día Chile³², que tiene algunos estudios de investigación formativa^{33,34} y promueve el consumo de frutas y verduras a través de distintas estrategias, incluyendo su distribución en algunas escuelas, en coordinación con instituciones del sector público y empresas privadas.

Conclusión

Los resultados de este estudio, junto al diagnóstico de las distintas iniciativas existentes y las que se implementarán para el cumplimiento de la Ley 20.606, podrían facilitar el desarrollo de estrategias de comunicación e implementación de acciones efectivas para promover el cumplimiento de los mensajes de las GABA en el país.

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Original / *Obesidad*

Effect of a weight loss program in obese adolescents; a long-term follow-up

Ilonka Rohm, Michelle Schaarschmidt, Hans R. Figulla, Michael Lichtenauer, Björn Goebel, Marcus Franz and Christian Jung

Friedrich-Schiller-University. Clinic of Internal Medicine I. Jena. Germany.

Abstract

Objectives: Obesity during adolescence is an increasing health problem in industrial countries. The co-morbidities associated with obesity include important metabolic diseases.

Methods: To analyze the effect of a weight-loss program, we recruited 12 obese, male adolescents before entering this program. We determined body weight measures at baseline, 6-week and 36-month follow-up. Also, the long-term changes of blood pressure, HbA1c, and CRP were evaluated. Twenty healthy age-matched adolescents served as controls.

Results: Within the intervention group ((body mass index [BMI, kg/m²] > 95th percentile for age and sex, age 13-17 years) the BMI and BMI-standard deviation score [SDS] were significantly reduced in the 6-week follow-up after completing the weight loss program. However, the significant weight-reduction effect was not persistent until the 36-month follow-up.

Conclusion: The 6-week weight-loss program had beneficial short-term effects on body weight, BMI, and BMI-SDS in obese adolescents, but these effects could not be maintained until the 36-month follow-up.

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Key words: Adolescent. Long-term effects. Obesity. Weight loss. Weight reduction programs.

EFFECTO DE UN PROGRAMA DE PÉRDIDA DE PESO EN ADOLESCENTES OBESOS; SEGUIMIENTO A LARGO PLAZO

Resumen

Objetivos: La obesidad durante la adolescencia es un problema de salud creciente en los países industriales. Las co-morbilidades asociadas a la obesidad conllevan importantes enfermedades metabólicas.

Métodos: Para analizar el efecto de un programa de pérdida de peso, seleccionamos a 12 adolescentes varones obesos antes de entrar en este programa. Determinamos las mediciones de peso corporal al inicio del programa y en los seguimientos a las 6 semanas y a los 36 meses. También se evaluaron los cambios a largo plazo de tensión arterial, HbA1c y PCR. Igualmente se seleccionó a veinte adolescentes sanos de la misma edad que sirvieron como grupo de control.

Resultados: Dentro del grupo de intervención ((índice de masa corporal [IMC, kg/m²] > percentil 95 para edad y sexo, 13-17 años) el IMC y la puntuación de la desviación estándar sobre el IMC [SDS] se vieron significativamente reducidos en el seguimiento de 6 semanas tras completar el programa de pérdida de peso. Sin embargo, el efecto de reducción de peso significativa no fue persistente hasta el seguimiento a los 36 meses.

Conclusión: El programa de pérdida de peso de 6 semanas tuvo efectos beneficiosos a corto plazo en el peso corporal, IMC y en el IMC-SDS en adolescentes obesos, pero estos efectos no se pudieron mantener hasta el seguimiento a los 36 meses.

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Palabras clave: Adolescente. Efectos a largo plazo. Obesidad. Pérdida de peso. Programas de pérdida de peso.

Correspondence: Christian Jung.
Clinic of Internal Medicine I.
Friedrich-Schiller-University.
Erlanger Allee 101.
D-07747 Jena. Germany.
E-mail: christian.jung@med.uni-jena.de

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Abbreviations:

Ao: Aorta.
BMI: Body mass index.
BMI-SDS: Body mass standard deviation score.
BP: Blood pressure.
CHD: Coronary heart disease.
CKD: Chronic kidney disease.
CRP: C-reactive protein.
EF: Ejection fraction.
FS: Fractional shortening.
FU: Follow-up.
HDL: High-density lipoprotein.
IVS: Intraventricular septum.
LAD: Left atrium diameter.
LDL: Low-density lipoprotein.
LP(a): Lipoprotein a.
LVD: Left ventricular diameter.
LVPW: Left ventricular posterior wall.

Introduction

Over the past years, pediatric and adolescent obesity has reached epidemic proportions in industrial countries throughout the whole world. The National Health and Nutrition Examination Study (NHANES) showed that in the USA almost 17% of children and adolescents are considered obese and 32% overweight or obese.¹ In Germany, data obtained from 2003-2006 showed that 15% of 3-17 years-olds are overweight, and 6,3% are obese.² This is an increase in the prevalence of overweight and obesity by 50% with respect to the 1980s and 1990s. The study also demonstrated that the percentage of overweight persons increased from < 1% of the 3-6 years-olds to 15% of the 7-10 years-olds to 17% of the 14-17 years-olds. According to the WHO classification, overweight is defined as a body mass index (BMI) > 25 kg/m² and obesity as a BMI > 30 kg/m² for adults (> 19 years of age), and for children aged 2 to 19 years, overweight is defined as a BMI between the 85th and 95th percentile, while obesity is defined as a BMI at or above the 95th percentile for children of the same age and sex.³

Chronic obesity in adolescence persisting to adulthood causes —besides social consequences like social discrimination, and low self-esteem— an increased risk to develop diseases that involve different apparatuses, for example sleep apnea, asthma, steatohepatitis, and musculoskeletal diseases like slipped capital femoral epiphysis, and blount's disease. It also increases cardiovascular risk factors⁴ and causes metabolic diseases like hypertension, type 2 diabetes mellitus, and dyslipidemia.⁵ For diabetes it is shown that the risk to develop this metabolic disease is particularly high in individuals who were obese as adolescents compared to those with adult-onset obesity.⁶ This increased risk to develop metabolic diseases associated with obesity might be one of the reasons for a correlation of the BMI of persons between 7 and < 18 years and the risk to develop coronary heart disease (CHD).^{7,8}

Besides its consequences for the individual, obesity raises enormous costs for the health system of developed countries. A recent study in the USA showed that childhood obesity causes besides hospitalization for comorbidities of obesity⁹ also increased expenditures for additional outpatient/emergency room visits or prescription drug expenditures. Data from the Medical Expenditure Panel Survey from 2002-2005 demonstrated that elevated BMI in childhood was associated with 14.1 billion additional USD only for non-hospitalization expenditures. Furthermore, it has been shown that adolescent obesity is strongly associated with persistent adulthood obesity¹⁰ which represents ongoing health risks – and ongoing health costs. For all these mentioned reasons it is particularly important to act against obesity in childhood and adolescence. Besides putting effort in health education of the child or adolescent itself, it is also fundamental to include the children's environment, especially raise their parents' or caregivers' awareness for proper nutrition and healthy habits.¹¹

In Germany, it is possible for obese children and adolescents to take part in outpatient or inpatient weight loss programs financed by the national health system. In the year 2001, 5950 weight loss programs were financed by the German government for children and adolescents up to 19 years.¹² Considering these enormous health costs, it is important to have a proven long-term effectiveness of these programs. While different lifestyle intervention programs addressing adults have been evaluated, so far there are only few studies targeting children and adolescents. Whereas for adolescents there are different studies showing significant weight-reduction effects of intervention programs in short-term follow-ups,¹³ there are only few studies about the long-term effects. A recent study was published by Lloyd-Richardson et al.¹⁴ who provide 24-month follow-up data from a randomized trial of two 6 month group-based behavioral weight loss programs for obese adolescents in the USA. It has been demonstrated that these programs were effective at reaching and maintaining weight reductions in 13-16 years-old adolescents through a 24-month follow-up. In a 4-years follow-up, Kubicky et al.¹⁵ presented a significant, but slight reduction in BMI-SDS from 2.49 to 2.33.

Despite different results showing some long-term effects of weight intervention programs, the effectiveness of these programs needs to be further investigated because of a lack of quality management for inpatient weight loss programs resulting in similar program structures. Thus, the aim of the present study was to examine the long-term outcome (36 months) of a 6-week inpatient weight loss program for adolescents.

Methods

In this observational study 12 obese adolescents (intervention group, median weight 96 kg; 82-111 CI) and 20 adolescents with normal BMI (control group, median

weight 64 kg; 60-68 CI) were included. Participants were aged 13 to 17 years, male, and Caucasian. The adolescents of the obese group had a BMI above the 95th percentile (mean BMI-SDS 2.4; 2.1-2.7 CI) at time of study enrollment. They were recruited from a specialized local rehabilitation hospital. As a control group, voluntary, obviously healthy adolescents from schools of the same geographic area (Jena, Germany), were recruited. Written informed consent was obtained from the adolescent and at least one parent. The study protocol was approved by the ethics committee of the University of Jena and is in accordance with the Helsinki Declaration II. For all participants the following characteristics were recorded at study inclusion: age, height, weight, BMI, waist circumference, hip circumference, hip/waist-ratio, heart rate, blood pressure, sports habits, and family history. Exclusion criteria were any sign of disease or medications that potentially influence body weight.

In the 6-week weight loss program the obese participants attended, importance was attached to nutritional education, physical activity, and behavior modification. At admission, adolescents had to absolve a fitness test. According to the fitness test results, patients had to attend obesity-sports and swimming activities: swimming (2x/week), bicycle ergometer (2-3x/week), sports in a gym or outdoor (3x/week), 1x adolescents' favorite sports, in summary at least 6 h/week. These activities were supervised by a sports teacher. Also, every day before breakfast the participants had to do 15 minutes morning sports. Additionally, there were leisure activities like hiking attended by pedagogues. As possible, heart rate was measured to determine the sports intensity. Nutritional intervention and nutritional education was based on the food guide pyramid. Adolescents were taught how much the recommended intake for each food group according to their age is. Therefore, they had to weigh everything they ate during this 6-week program. Nutritional education was presented by a dietitian. Participants attended 90-minutes nutrition classes each week and additionally informal meetings discussing the eaten food once a week. During these classes adolescents were taught to shop and cook in a healthy manner, and learned how to estimate the calories of different foods properly. Medical ward rounds were held by a medical doctor for endocrinology. If necessary, psychologists were available to support adolescents' progress. In addition to this support provided for the adolescents themselves, the clinic offered educational training in physical exercise, nutrition, and behavioral habits for parents.

Data achievement

Data of 12 obese adolescents were obtained at the time of inclusion and at a 6-week follow-up. In addition all participants were invited to a 36-month follow-up and contacted via telephone. Five adolescents refused to take part in the long-term follow up resulting in data of 7 obese adolescents at 36 months. Data of adolescents with

normal weight were obtained as control group data at the time of inclusion. Basic clinic data were collected from adolescents and parents including age, sex, weight, and height. Participants' weight and height were measured by the study team. The height (in meters) was determined without shoes using a stadiometer calibrated in 0.1-cm intervals. Participants' weight (in kilograms) was measured without shoes wearing a light gown using a medical weight scale, calibrated before each weight. Weight and height were used to calculate BMI (kg/m²). BMI-standard deviation score (BMI-SDS) was calculated according to current guidelines using German charts (16). Briefly, the formula $BMI-SDS = ([BMI/M(t)] L(t) - 1)/L(t) * S(t)$ was used. $M(t)$ is the age- and sex-specific BMI median. $L(t)$ and $S(t)$ are age- and sex-specific calculation variables available in charts. Blood pressure was measured three times by a single trained observer using a conventional blood pressure analyzer after participants sat still for at least 5 minutes. Blood samples for routine laboratory were obtained after a 8-hour overnight fast for measurement of serum glucose, total cholesterol (mmol/l), HDL cholesterol (mmol/l), LDL cholesterol (mmol/l), and triglycerides (mmol/l), lipoprotein (a) (mg/l), high sensitive CRP (CRP) (mg/l), and white blood count differential in the Department for Clinical chemistry of the University Hospital Jena.

Statistical analysis

Analyses at baseline included all participants ($n = 32$), at the end of the 6-week weight loss program data were also obtained from all obese adolescents. 58% ($n = 7$) of the obese group consented to take part in the follow-up examination 36 months after completing the weight loss program. Statistical analysis was performed by using Sigma Plot Version 12.0 (Systat Software Inc.). Paired t-tests, One Way ANOVA of repeated measurements, Fisher Exact Test, and correlation (Spearman's rank correlation coefficient) were used to evaluate changes in body weight across the time (baseline, 6 weeks, 36 months), and the differences between the two groups. Normal distribution was tested with the Shapiro Wilk Test. Not normally distributed continuous variables were compared by the Signed Rank Test. Statistical significance was assigned at the 0.05 level of probability.

Results

The baseline parameters of 32 adolescents enrolled in the present study are summarized in table I. As expected, adolescents in the obese group had a significantly higher body weight (1.5-fold), BMI, and BMI-SDS (all: $p < 0.001$). The obese group also had higher waist (1.4-fold) and hip (1.3-fold) circumferences compared to the control group. Interestingly, the waist-to-hip ratio was almost equal in both groups. The waist index was significantly, 1.4-fold higher in the obese

Table I
Characteristics of the study groups at baseline. Data presented as mean ($\pm$ SEM) or id Normality Test (Shapiro Wilk-Test) failed as median (25-75% CI).

	Control group (n = 20)		Obesity group (n = 12)		p value
	Median	25-75% CI	Median	25-75% CI	
Age (y)	15.0	15.0-16.0	15.0	14.0-16.5	n.s.
Body Weight (kg)	64.5	58.3-68.0	97.0	85.3-107.8	<0.001
BMI (kg/m ²)	20.1	18.9-21.9	31.7	28.3-34.7	<0.001
BMI-SDS	-0.08	$\pm$ 0.69	2.43	$\pm$ 0.49	<0.001
Waist circumference (cm)	73.0	68.3-74.8	102.0	91.3-107.8	<0.001
Hip circumference (cm)	82.5	78.3-84.8	109.0	102.0-119.0	<0.001
Waist-to-hip-ratio	0.88	$\pm$ 0.04	0.90	$\pm$ 0.05	n.s.
Waist index	41.0	39.0-42.2	59.1	52.6-63.1	<0.001
Heart rate (/min.)	80	$\pm$ 14	79	$\pm$ 12	n.s.
BP sys (mmHg)	120	120-130	134	123-143	n.s. (p = 0.07)
BP dias (mmHg)	70	60-80	71	63-78	n.s.
Total cholesterol	4.1	$\pm$ 0.92	4.0	$\pm$ 0.92	n.s.
HDL (mmol/l)	1.2	1.1-1.5	1.1	0.9-1.2	0.01
LDL (mmol/l)	2.2	1.9-2.9	2.6	2.0-3.1	n.s.
LDL/HDL	1.8	1.3-2.5	2.5	2.2-3.1	0.03
Lp(a) (mg/l)	60	30-126	193	124-314	0.02
TG (mmol/l)	0.9	0.8-1.2	0.8	0.6-1.1	n.s.
HbA1c (%)	5.1	4.9-5.2	5.2	5.2-5.3	0.03
CRP (mg/l)	0.1	0.1-0.1	1.5	0.7-7.3	<0.001

BP: blood pressure, HDL: high density lipoprotein, LDL: low density lipoprotein, LP(a) Lipoprotein a. n.s.: not significant.

group with respect to the control group. Also, they had a slightly but significantly elevated HbA1c. There was a trend to a higher systolic blood pressure in the obese group ($p = 0.07$). Besides that, they presented an altered cholesterol profile: The high-density lipoprotein (HDL) was significantly lower than in the control group and this led to a significantly altered HDL/LDL ratio. The HDL/LDL ratio was 1.8 in the control group and 2.5 in the obese group. The lipoprotein A was significantly, 3.2 -fold higher in obese adolescents. Moreover, an elevated, 15-fold higher CRP in the obese group compared to the control group was detectable suggesting a higher pro-inflammatory status.

Analyzing exercise habits (table II), significantly more participants (2.1-fold) of the control group did sports. The control group also spent significantly more time doing sports (50-fold). Analyzing nutritional habits, there was no significant difference in the number of warm meals/week and the adolescents' impression of their parents paying attention for regular meals. Looking at the participants' families, the participants' mothers had a significantly higher BMI in the obese group. The BMI of the adolescents' mothers was 23.1 kg/m² in the control group and 29.0 kg/m², in the obese group, showing that the mothers of participants with normal weight are also of normal weight and mothers of obese participants are often also overweight. Also, the parents of the treatment group are significantly younger than the parents of the control group. In addition, there was a higher emergence of cardiovascular diseases in the participants' relatives of

first or second degree: They had significantly more often diabetes mellitus, hypertension, gout, and a trend to a higher emergence of hyperlipidemia. Concerning the academic education of the participants' parents, there was a higher educational level of the mother visible in the control group than the obese group. The mothers in the control group had absolved more often university studies. However, this did not reach significance. Interestingly, adolescents of the obese group had significantly better school grades (average school grade 2.8 ± 0.5 in the obese group, 2.2 ± 0.7 in the control group, $p = 0.04$). There was no difference visible in the use of television or computer during their free time in both groups.

In correlation analyses, we were able to show significant correlations between CRP and BMI-SDS ($r = 0.7$, $p < 0.001$, fig. 1) or BMI ($r = 0.7$, $p < 0.001$). This reflects a higher inflammatory state in obesity. Interestingly, in the performed correlation analyses, a correlation between systolic blood pressure and BMI-SDS ($r = 0.6$, $p = 0.009$) or BMI ($r = 0.6$, $p = 0.004$) could be noticed, which demonstrates a correlation between different cardiovascular risk factors.

Echocardiographic parameters

Additionally, echocardiographic data were obtained (table IV). The intraventricular septum thickness (diastolic) (IVSd) was significantly higher in the obesity group than in the control group. Also, the diameter of

Table II
Behavioural habits of the study groups. Data presented as mean ($\pm$ SEM) or if Normality Test (Shapiro-Wilk-Test) failed as median (25-75% CI).

	Control group		Obesity group		p value
	Median	25-75% CI	Median	25-75% CI	
Smoking	15%		8%		n.s.
Sports	90%		42%		0.006
Sports (hours/week)	5	1.5-9.0	0.1	0.1-1.8	0.04
School bread/week	4	0-5	5	0-5	n.s.
Warm meal/week	7	4-7	7	2-7	n.s.
Parents attention for nutrition	70%		92%		n.s.
BMI mother (kg/m ²)	23.1	21.6-27.3	29.0	24.2-36.2	0.04
BMI father (kg/m ²)	25.3	24.5-28.5	25.9	23.5-30.5	n.s.
Age mother (y)	42.5	$\pm$ 4.2	36.7	$\pm$ 3.5	0.004
Age father (y)	44.7	$\pm$ 4.2	40.4	$\pm$ 4.3	0.03
Father university studies	10%		8%		n.s.
Mother university studies	40%		8%		n.s.
Father unemployed	5%		0%		n.s.
Mother unemployed	10%		25%		n.s.
Siblings	1	1-1	1	0-1	n.s.

BMI: Body mass index. n.s.: not significant.

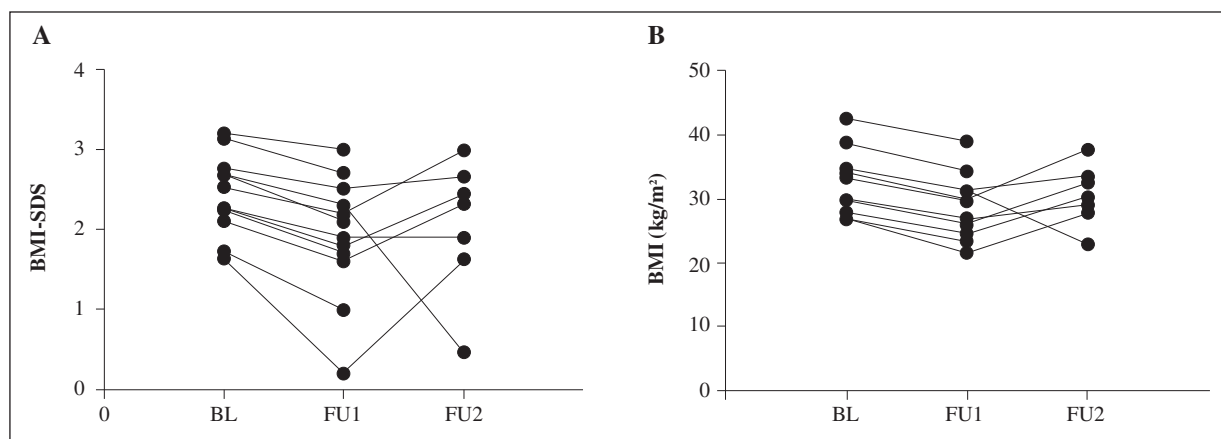


Fig. 1.—BMI-SDS (A) and BMI (B) follow-up of the participants in the obesity group at baseline (BL), the 6-week follow-up (FU1), and 36-month follow-up (FU2).

Table III
Family history. Emergence of diseases in the participants' relatives of first or second degree

	Control group	Obesity group	p-value
Hypertension	25%	75%	0.01
Diabetes mellitus	5%	67%	<0.001
Hyperlipidemia	1%	25%	n.s. (0 = 0.07)
Gout	5%	42%	0.02
CKD	10%	25%	n.s.
CHD	15%	25%	n.s.

CKD: chronic kidney disease; CHD: coronary heart disease; n.s.: not significant.

the left atrium (systolic) (LADs) was significantly higher in obese adolescents. These differences reflect first changes in the heart structure that reflect beginning left ventricular hypertrophy.

Effect of a weight loss program

The 12 recruited obese adolescents took part in a weight loss program (median duration time 5.8 weeks) and all of them completed it. 7 obese adolescents (58%) of the obese group attended the 36-month follow-up. The adolescents that dropped out of the study had similar anthropometric data compared to those who completed the follow-up.

Table IV
Echocardiographic parameters of the two study groups

	Control group		Obesity group		<i>p</i> value
	Median	25-75% CI	Median	25-75% CI	
Ao (mm)	29.4	± 2.5	30.7	± 3.6	n.s.
LADs (mm)	33.2	± 4.0	39.2	± 3.7	0.005
IVSd (mm)	9.3	± 1.3	10.6	± 1.6	0.034
LVPWd (mm)	10	90-11.0	9.0	9.0-11.3	n.s.
IVSs (mm)	12.2	± 1.5	12.8	± 1.2	n.s.
LVPWs (mm)	15.0	13.0-16.0	16.5	13.0-17.0	n.s.
LVDd (mm)	47.7	± 4.2	49.5	± 4.4	n.s.
LVDs (mm)	29.9	± 4.9	32.0	± 3.6	n.s.
FS	0.4	± 0.06	0.4	± 0.06	n.s.
EF	0.68	± 0.07	0.65	± 0.07	n.s.

Ao: Aorta; LADs: left atrium diameter systolic; IVSd: intraventricular septum diastolic; LVPWd: left ventricular posterior wall diastolic; IVSs: intraventricular septum systolic; LVPWs: left ventricular posterior wall systolic; LVDd: left ventricular diameter diastolic; LVDs: left ventricular diameter systolic; FS: fractional shortening; EF: ejection fraction; n.s.: not significant.

Short-term weight changes

After completion of the 6-week weight loss program, a significant decrease in all parameters reflecting weight status could be detected. There was a reduction in median weight from 97 kg to 87.5 kg ($p < 0.001$, table V) and a significant decrease in BMI from 31.7 to 28.4 ($p < 0.05$) from baseline to follow-up. BMI-SDS decreased from median 2.4 to 2.0 ($p < 0.001$) after the 6-week program.

Long-term weight changes

7 adolescents of the obese group attended the 36-month follow-up. In the obese group, 36-month follow-up data reflecting body weight changes revealed a relevant increase in body weight, BMI, and BMI-SDS compared to the 6-week follow-up. Anyway, there was a relevant increase in BMI-SDS from 2.0 after completion of the weight loss program to 2.3 at the 36-month follow-up. This change did not reach the level of significance because of the reduced

number of obese adolescents attending the long-term follow-up. Comparing the BMI-SDS as the most reliable parameter reflecting body weight status over time and growth process, the BMI-SDS almost remained the same at baseline and 36 months after completion of the weight loss program (2.3 at 36-month follow-up, 2.4 at baseline). This shows that the relevant weight-reducing short-term effect of the weight loss program could not be maintained to the long-term follow-up. The BMI increased significantly again comparing the 6-week follow-up and the 36-month follow-up (from median 28.4 to 30.6, $p < 0.05$). Also, in the 36-month follow-up, different cardiovascular risk factors (blood pressure, lipid profile, HbA1c, CRP) did not differ significantly from those at the time of inclusion.

Discussion

In summary, significant differences in baseline characteristics were found for obese and non-obese adolescents, including an altered lipid profile, an increased CRP reflecting a higher inflammatory state, and higher

Table V
Changes in parameters reflecting body weight status in the obesity group

	Baseline (BL)		6-week FU (FU1)		<i>p</i> -value FU1: BL	36-month FU (FU2)		<i>p</i> -value FU2: FU1	<i>p</i> -value FU2: BL
	Median	25-75% CI	Median	25-75% CI		Median	25-75% CI		
N	12		12			7			
Age (y)	15.0	14.0-16.5	15.0	14.0-16.5	n.s.	18	16-18		
Body weight (kg)	97.0	85.3-107.8	87.5	69.8-97.8	<0.001	105.4	92.3-117.0	n.s.	n.s.
BMI (kg/m ²)	31.7	28.3-34.7	28.4	25.1-31.3	<0.05	30.6	27.8-33.6	<0.05	n.s.
BMI-SDS	2.4	2.1-2.7	2.0	1.6-2.5	<0.001	2.3	1.6-2.7	n.s.	n.s.

BMI: body mass index; BMI-SDS: body mass index standard deviation score; n.s.: not significant.

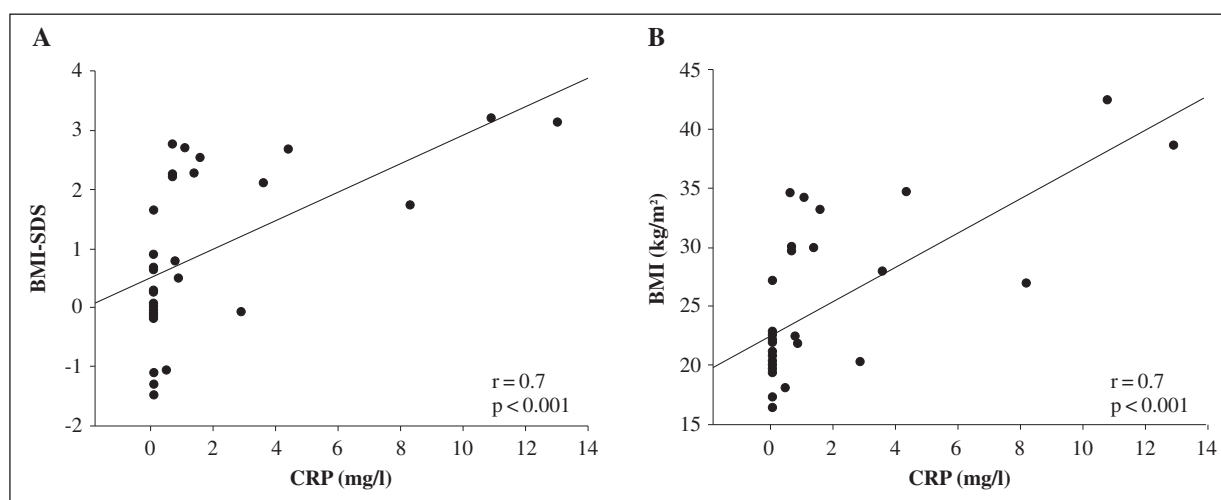


Fig. 2.—Correlations between BMI-SDS (A) and BMI (B) with CRP. r correlation coefficient, p : level of probability.

values for HbA1c and blood pressure. This confirms earlier studies published.¹⁷⁻²² The data obtained reflect a higher cardiovascular risk factor profile in obese adolescents and might explain partially why already childhood BMI is positively correlated with coronary heart disease, and stroke in later life.^{7,23} This is further supported by the obtained echocardiographic parameters indicating early structural changes caused by obesity. A higher intraventricular septum thickness and a larger left atrium are findings typical for left ventricular (LV) hypertrophy. This observation is in concordance with former studies that showed that the thickness of the LV correlates with BMI, and LV hypertrophy has been shown to occur more often in obesity.^{24,25} As expected, participants of the control group spent significantly more time doing sports than the obese group. This finding supports the theory that one of the main reasons why obesity is an increasing problem of the presence is a decrease in physical activity and an increase in sedentary habits.²⁶ Other predisposing factors for obesity is a low parental level of education, and a low parental income.²⁷ This is reflected in the results of the current study which show a higher number of absolved university studies of the participants' mothers in the control group than in the treatment group. Considering all these findings long-lasting weight loss effects are of central importance to ameliorate the consequences of obesity in early life.

However, our small observational, non-randomized study shows that attendance at the 6-week weight loss program did not lead to a significant long-term reduction of body weight of the included adolescents. A significant weight loss could be noted directly after attendance of this program, but as the adolescents leave the clinic, they gain weight again. Due to the limited number of subjects our study results have to be interpreted with some limitations. Although one can assume that the adolescents that dropped out the study show similar developments in their weight, the poor reten-

tion rate reduces the power of our thesis that questions the long-term effectiveness of weight loss programs. On the other hand, the obtained data clearly shows that there was no long-term detectable after three years.

Former studies investigating the effectiveness of weight management programs showed conflicting results, some presenting significant reductions in body weight and body fat,^{14,15,28} others demonstrating that the weight reduction could not be maintained in long-term follow-up.^{29,30} It is important to find the reasons for this contradiction. Analyzing the methodic part of the publications, it is not possible to get a comprehensive view about the weight loss programs investigated. In the future, different programs with different methodic approaches should be compared and further evaluated, possibly using randomization comparing different protocols.

It is also important to evaluate the weight-reducing effect of intervention programs with respect to different patients' ages. For example, a former study showed differences in the long-term maintenance (3 years) of weight-reducing effects for an outpatient intervention. There were significant reductions in BMI-SDS observed for severely obese children, but not adolescents.³¹

Moreover, integration of the participants' families, especially their mothers, seems to be extraordinary important to give rise to long-term success.³² A former study showed that the mother's characteristics are more important than those of the father in children's obesity and weight loss.³³ This theory is supported by the observation of the current study that overweight of mothers is associated with higher emergence of obesity in adolescents.

Obviously, a quality management for weight loss programs resulting in homogeneous standards is indispensable to guarantee similar effects for different programs. In the future, through a more detailed examination of current weight loss concepts standardized programs should be created to achieve long-term success. Generating effective weight loss programs for

adolescents is critical to leading to health improvement in the adulthood because there is simply a lack of alternatives. For example, current existent medical treatment for obesity is limited. Orlistat is the only drug available for long-term use for weight-reduction. It leads only to a very slight reduction of weight, some studies do not find a significant reduction of weight at all.³⁴ Also surgical interventions are left for severe obesity because of their surgical risks and adverse effects. For these reasons, conservative treatment of obesity gains enormous importance and needs to be put in the focus of health questions.

In conclusion, existing weight loss programs should be critically analyzed in the future to develop a similar standard with proven long-term success within different intervention programs to fight the growing health threat of obesity, especially in early life.

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Original / *Obesidad*

ROC curves of obesity indicators have a predictive value for children hypertension aged 7-17 years

Tai-shun Li¹, Wen-jie Sun², Ming-wei Wei¹, Shi-hong Chen¹, Peng Wang¹, Xu-lin Wang¹, Lian-ping He¹ and Yu-feng Wen¹

¹School of Public Health. Wannan Medical College. Wuhu 241002. China. ²Department of Public Health and Tropical Medicine. Tulane University. New Orleans. LA 70112. USA.

Tai-shun Li and Wen-jie Sun contributed equally to this work.

Abstract

Objective: The aim of the study is to examine the distribution of integrated covariate and its association with blood pressure (BP) among children in Anhui province, China, and assess the predictive value of integrated covariate to children hypertension.

Methods: A total of 2,828 subjects (1,588 male and 1,240 female) aged 7-17 years participated in this study. Height, weight, waistline, hipline and BP of all subjects were measured, obesity and overweight were defined by an international standard, specifying the measurement, the reference population, and the age and sex specific cut off points. High BP status was defined as systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) $\geq$ 95th percentile for age and gender.

Results: Our results revealed that the prevalence of children hypertension was 11.03%, the SBP and DBP of obesity group were significantly higher than that of normal group. Anthropometric obesity indices such as body mass index (BMI) were positively correlated with SBP and DBP. Integrated covariate had a better performance than the single covariate in the receiver-operating characteristic (ROC) curve, the cut-off value; the sensitivity and the specificity of the integrated covariate were 0.112, 0.577, 0.683, respectively.

Conclusion: Integrated covariate is a simple and effective anthropometric index to identify childhood hypertension.

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Key words: Childhood hypertension. Obesity receiver-operating characteristic (ROC) curve.

CURVAS ROC DE LA OBESIDAD EN LOS INDICADORES TIENEN UN VALOR PREDICTIVO PARA NIÑOS DE ENTRE 7 Y 17 AÑOS HIPERTENSIÓN

Resumen

Objetivo: El objetivo del estudio es examinar la distribución de las covariables integrado y su asociación con la presión arterial (PA) entre los niños en la provincia de Anhui, China, y evaluar el valor predictivo de covariables integrado a los niños la hipertensión.

Métodos: Un total de 2.828 sujetos (1.588 macho y 1.240 hembra) de 7 a 17 años participaron en este estudio. Altura, peso, cintura, hipline y BP de todos los sujetos fueron medidos, la obesidad y el sobrepeso se han definido por una norma internacional, especificando la medición, la población de referencia, y la edad y sexo los puntos de corte. La condición de alta presión se define como la presión arterial sistólica (PAS) y/o presión arterial diastólica (PAD) $\geq$ percentil para edad y sexo.

Resultados: Nuestros resultados revelan que la prevalencia de niños la hipertensión fue 11,03%, el SBP y DBP de obesidad grupo fueron significativamente más alta que la de grupo normal. Los índices de obesidad, tales como el índice de masa corporal (IMC) se correlacionaron positivamente con SBP y DBP. Integrado covariable tuvo un mejor rendimiento que la covariable en la curva de características operativas del receptor (ROC), el valor de corte, la sensibilidad y la especificidad de las covariables fueron integrados 0,112, 0,577, 0,683, respectivamente.

Conclusión: Integrado covariable es un simple y eficaz para identificar a la niñez índice antropométrico hipertensión.

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Palabras clave: Hipertensión. Obesidad infantil de la curva de características operativas del receptor (ROC).

Correspondence: Yu-feng Wen.

School of Public Health.
Wannan Medical College.
Road No.22, WenChang Xi, Wuhu city, Anhui province.
241002 China.
E-mail: wyf@wnmc.edu.cn

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Introduction

Hypertension is one of the public health which have severely harm to human.^{1,2} In recent years, hypertension is prevalence among young adults, previous study showed that the overall prevalence of essential hypertension is vary from 1% to 5%.^{3,4} Childhood hypertension can lead to serious health problems,^{2,5,6} such as leading to adult hypertension, and adults' left ventricular hypertrophy, which is seen as many as 41% of patients with children hypertension.^{7,8} Previous studies showed that overweight and obese children face an approximately threefold higher risk for essential hypertension than do non-obese children.^{9,10} The obesity of kids and teenagers had become an important public health problem.¹¹

The prevalence of overweight and obesity among children and adolescents is increasing worldwide.^{12,13} Appropriate early-stage diagnosis and intervention of hypertension in children and adolescents are important for reducing the risk of hypertension related disorders in adults.^{2,6} Identifying hypertension in children and adolescents is more complicated than in adults, because childhood hypertension is based on a set of age, gender, and height specific references in systolic blood pressure (SBP) and diastolic blood pressure (DBP).⁴ Thus, a simplify method to diagnostic children hypertension is more important. Many previous studies focus on the relations between the general or central obesity and BP to explore the diagnostic criteria of children hypertension.¹⁴⁻¹⁶

BMI is widely used as a measurement to define obesity, the potential value to predict BP remains debatable.^{17,18} Other measurements, WC and waist-to-height ratio (WHtR), as indicators of abdominal fat mass, may have close relationship with BP in children. Moreover, some studies demonstrated that the ratio of waist circumference to height (WHR) was even superior to waist circumference (WC) and body mass index (BMI) to predict hypertension in children,^{19,21} but it remains dispute.

The aim of the study is to examine the distribution of integrated covariate and its association with blood pressure (BP) among children in a large population in Anhui and to assess the predictive value of integrated covariate to children hypertension.

Methods

A cross-sectional survey with representative sample of children aged 7-17 years was conducted in 2013 from Anhui province, China. A cluster sampling method was used to sample the participants. With city as the sampling unit, first, 2 cities were randomly selected from 22 cities. 5 primary schools were then randomly selected from the cities. Finally, about 2,828 participants aged 7-17 years were selected from 3,000 school children (Response rate was 94.4%). Written consent form was obtained from parents or guardians of the children.

Measurements

All measurements were conducted by a team of trained technicians in each of the selected districts and finished by the same type of apparatus and followed standard procedures. In addition, demographic, socioeconomic data were collected by an interviewer through questionnaire.

BP measurements

All BP measurements were recorded using an aneroid sphygmomanometer with the participants in a comfortable seated position and the right arm fully exposed and resting on a supportive surface at heart level. A bladder was selected with a width covering at least two thirds of the upper arm and a length exceeding the biceps circumference by at least 50%. The cuff was inflated to 20 mmHg over the pressure that occluded the pulse at the wrist, the stethoscope was placed over the antecubital fossa, and the cuff was deflated. The onset of the first Korotkoff sound was used to measure SBP, whereas the fifth was used for DBP. Two readings taken at least 5- to 10-min apart were obtained for each participant, and the mean number of the two measurements was calculated.²²

Anthropometric measurements

Height, weight, hipline and waistline of children were measured by using a calibrated stationmaster (Shorr Productions, Olney, MD) and scale (Seca model 881, Seca Corporation, Hanover, MD). All anthropometric measurements (weight, height, hipline, waistline) were performed according to standardized method,²³⁻²⁵ e.g. Height without shoes was measured by Metal column height-measuring by stands to the nearest 0.1 cm. WC was measured midway between the lowest rib and the superior border of the iliac crest with a non-elastic measuring tape at the end of normal expiration to the nearest 0.1cm. Hipline was measured at the widest level over the great trochanters using a plastic flexible tape to the nearest 0.1 cm. Body weight was measured using a SALTER 920 digital weighing scale (SALTER Ltd., Ton bridge, UK) to the nearest 0.1 kg after an overnight fast and with indoor light clothing. BMI was calculated as weight in kilograms divided by height squared in meters (kg m^{-2}). WHR and WHtR were calculated as WC divided by hipline and WC divided by height, respectively.

Definition

Children hypertension

Children hypertension was defined by China national reference standard: systolic blood pressure or

Table I
Comparison of the obesity indicators between hypertensive and non-hypertensive

Obesity indicators	Male (n = 1,588)			Female (n = 1,240)		
	Non-hypertensive	Hypertensive	p	Non-hypertensive	Hypertensive	p
Weight (kg) ^a	50.26 ± 13.22	59.66 ± 16.33	0.000	46.53 ± 10.25	51.65 ± 12.15	0.000
Waistline (cm) ^a	69.13 ± 9.09	75.62 ± 11.05	0.000	65.71 ± 7.17	68.86 ± 9.08	0.000
BMI (kg/m ²) ^a	20.01 ± 3.57	22.49 ± 4.12	0.000	19.45 ± 3.02	21.13 ± 3.99	0.000
WHR ^a	0.83 ± 0.07	0.85 ± 0.09	0.000	0.78 ± 0.06	0.79 ± 0.06	0.323
WHTR ^a	0.44 ± 0.05	0.47 ± 0.06	0.000	0.42 ± 0.04	0.43 ± 0.06	0.000
Hipline (cm) ^a	83.57 ± 8.65	89.39 ± 10.20	0.000	84.16 ± 7.92	87.54 ± 8.77	0.000

The values in italics demonstrate that p values less than < 0.05 and consider to be statistically significant.

BMI: body mass index; WHR: waist-to-hipline ratio; WHTR: waist-to-height.

^aValues are given as mean ± SD (standard deviation).

Table II
The comparison of blood pressure between different genders and different groups

Groups	Male (n = 1,588)		Female (n = 1,240)	
	SBP (mmHg)	DBP (mmHg)	SBP (mmHg)	DBP (mmHg)
<i>BMI</i>				
Normal ^a	106.41 ± 11.90	59.71 ± 10.07	104.98 ± 10.75	61.75 ± 8.65
Overweight ^a	113.00 ± 13.06	62.06 ± 10.26	107.41 ± 12.17	61.84 ± 9.85
Obesity ^a	115.94 ± 14.77	63.26 ± 11.18	115.14 ± 12.28	66.50 ± 8.85
P	0.000	0.000	0.000	0.007

The values in italics demonstrate that p values less than < 0.05 and consider to be statistically significant.

^aValues are given as mean ± SD (standard deviation).

diastolic blood pressure equal or greater than the 95th percentile of the SBP or DBP with the same age and gender is regarded as hypertension.²⁶

Children obesity

Obesity and overweight were defined by an international standard, specifying the measurement, the reference population, and the age and sex specific cut off points.²⁷

Ethics Statement

The study was approved by the Ethical Review Board of the Wannan Medical College. Research protocols were approved by Wannan Medical College. All subjects provided a written informed consent after the research protocols were carefully explained to them.

Statistical Analysis

Independent sample t-tests were used to compare the related obesity index and blood pressure between male and female. Pearson's partial correlation coefficient was used to determine an association between variables and to verify significance. Analysis of variance

(ANOVA) was performed to compare blood pressure level according to BMI. Multiple logistic regression modules were used examined risk factors. ROC was used to compare the predictive value of anthropometric parameters to childhood hypertension and to determine the cutoff values. All analyses were performed by SPSS 13.0 (SPSS Inc., Chicago, IL, USA). *P* < 0.05 were considered statistically significant.

Results

A total of 2,828 subjects aged 7-17 years were conducted in our study, 56.15% (n = 1,588) were males, 59.87% (n = 1,693) were residing in urban areas. Mean age was 12.52 ± 1.83 years.

The prevalence of children hypertension were 11.03 % (males: 10.64%, females: 11.53%), the related obesity index was showed in table I; our results revealed that the related obesity index of children with hypertension was higher than hat of those childhood without hypertension. SBP and DBP of the obesity group were higher than over-weight group and normal group, differences of SBP and DBP among BMI groups are statistically significant (*P* < 0.05) (table II).

The correlations between the different anthropometric parameters and blood pressure are presented in

Table III
Relationship between SBP and DBP among anthropometric parameters and the differences among correlation coefficients

Variables	SBP		DBP		<i>p</i>
	Correlation coefficient (<i>r</i> ₁)	<i>p</i>	Correlation coefficient (<i>r</i> ₂)	<i>p</i>	
Weight	0.454	0.000	0.287	0.000	0.000*
Waistline	0.374	0.000	0.221	0.000	0.000*
Hipline	0.420	0.000	0.298	0.000	0.000*
BMI	0.351	0.000	0.203	0.000	0.000*
WHR	0.054	0.004	-0.022	0.248	0.153*
WHTR	0.161	0.000	0.064	0.000	0.000*

The values in italics demonstrate that *P* values less than < 0.05 and considered to be statistically significant.

**r*₁ compared to *r*₂.

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; WHR: Waist-to-hipline ratio; WHTR: Waist-to-height.

table III. All anthropometric parameters except WHR were significantly ($P < 0.05$) correlated with SBP and DBP in all students, males and females. Weight had the highest correlation with SBP and hipline had the highest correlation with DBP, The positive correlations observed between SBP among anthropometric parameters are stronger than DBP. The Z-test²⁸ among all correlations indicated differences are statistically significant except WHR ($P < 0.05$).

The AUCs of the anthropometric indices and integrated covariates in the prediction of children hypertension are shown in table IV. Of all students, the AUC of integrated covariates was significantly higher than that of anthropometric indices such as BMI, WC in the prediction of children hypertension. BMI, age and hipline were selected from many anthropometric indices by the multiple logistic regression analysis.

Then BMI, age and hipline were put into binary logistic regression model to identify independent risk factors for children hypertension and integrated covariates were made, as showed in table V. The single covariate in the area under the receiver-operating characteristic (ROC) curves is less than integrated covariates, and the optimal cut-off point of the integrated covariates is 0.08, at which the sensitivity is 0.64 and the specificity is 0.73. As showed in table VI.

Discussion

Our results show that traditional obesity anthropometric indices are positively associated with childhood hypertension. In all students, males and females the AUC of integrated covariates was significantly higher

Table IV
Comparison of the AUC (area under the curve) of anthropometric parameters

Variables	Male (<i>n</i> = 1,588)				Female (<i>n</i> = 1,240)			
	AUC	SE	<i>p</i>	95% CI	AUC	SE	<i>p</i>	95% CI
BMI	0.679	0.023	0.000	0.635-0.723	0.629	0.025	0.000	0.580-0.628
Waist	0.676	0.023	0.000	0.631-0.722	0.594	0.026	0.000	0.543-0.646
Hipline	0.682	0.022	0.000	0.638-0.723	0.608	0.026	0.000	0.558-0.658
Weight	0.672	0.023	0.000	0.627-0.717	0.629	0.026	0.000	0.577-0.680
WHR	0.577	0.024	0.001	0.529-0.624	0.527	0.027	0.299	0.474-0.580
WHTR	0.635	0.025	0.000	0.586-0.683	0.570	0.027	0.006	0.517-0.624
Integrated covariates	0.700	0.022	0.000	0.656-0.744	0.631	0.025	0.000	0.582-0.680

The values in italics demonstrate that *P* values less than < 0.05 and considered to be statistically significant.

AUC: Area under the Curve; SE: Standard error.

Table V
Detecting risk factors of hypertension with binary logistic regression

Covariates	<i>B</i>	<i>SE</i>	Wald χ^2	<i>OR</i>	<i>OR</i> 95% <i>CI</i>	<i>p</i>
Weight	0.224	0.009	12.952	1.032	1.014-1.050	0.000
Age	-0.201	0.042	22.663	0.819	0.755-0.889	0.000
Hipline	0.192	0.014	8.613	1.041	1.014-1.070	0.000
Constant		0.899	27.194			0.000

The values in italics demonstrate that *P* values less than < 0.05 and considered to be statistically significant.

SE: Standard error.

Table VI
The comparison between single covariates and integrated covariates of the diagnostic value for hypertension

Variables	AUC	SE	p	AUC 95% CI
Single covariates (BMI)	0.655	0.017	0.000	0.622-0.688
Integrated covariates	0.668	0.017	0.000	0.635-0.701

The values in *italics* demonstrate that P values less than < 0.05 and considered to be statistically significant

AUC: Area under the Curve; SE: Standard error.

than that of anthropometric indices in the prediction of children hypertension, integrated covariate is a simple and effective anthropometric index to identify children hypertension.

Our results on the correlations between the anthropometric parameters and blood pressure are in line with previous studies, which showed the BMI and WC had a association with hypertension.^{15,29} A study in South Asian adults found that WHtR had stronger association than BMI in prediction of hypertension.³⁰ However, our study showed that weight is better index than WHtR for perceiving childhood hypertension. The main problem of the study in South Asian adults was gender imbalance (0.395:0.605), which may decreased the representativeness of sample and also affected the result of study.

The possible reason maybe that there is an ethnic difference among different populations. In our study, most of participants were Han Chinese (98%). Additionally, South Asian people are thinner than Han Chinese of the same age. Some researcher found that identified optimal cutoffs of WHtR were not always equal to 0.5 from different regions.¹⁹

However, the study in Chinese adults in Beijing also found that the superiority of WHtR over weight in their association with hypertension. The participants in our study were children aged 7-17 years, which were the most important diversity compared to the study made in China. It is also well-known that WHtR is a simple alternative anthropometric index to measure abdominal obesity.³² But some indices such as weight and height were not to be constant, especially the index of weight were increased by a wide margin with age. The tendency of variances of weight were not included in WHtR, the early age nutritional environment is closely associated with body stature, weight was the most direct index for the growth of children and had the strongest association with obesity in children. So the maximal area under the curve is weight not WHtR.

Most of the studies have analyzed the single covariate evaluation of hypertension diagnosis value by BMI, waistline. But the significance to the diagnosis of hypertension by integrated covariates has not been reported. The integrated covariates united three obesity indices to assess diagnosis value for childhood hypertension by ROC curve. With regard to the currently recommended cutoff, integrated covariates had the strongest association with children hypertension, in both men and women, compared to the BMI, and hipline et al. The integrated

covariates area under the ROC curve is greater than the single covariate. It may be that the children hypertension is reflected by many anthropometric indices include height, weight, waistline, hipline and age. Integrated covariates are comprehensive enough variable for the diagnostic value of children hypertension; it can provide us with more accurate hypertension diagnosis value point.

There are several practical advantages of using integrated covariates for countries to prevent the epidemic tendency of children hypertension. First, it is easy to identify those at children hypertension risks with several anthropometric measurements. Second, the integrated covariates were united with several obesity indices, the diagnosis value for childhood hypertension are significantly higher than any other single index.

Despite being based on a very large study, our results have several limitations. First, the integrated covariate is a better marker of children hypertension in investigated children than the BMI. However, body composition of other children in different district may be different, so larger cross-sectional and prospective studies are needed to identify the applicability of integrated covariates for other district. Second, this is a cross-sectional analysis of an observational study. Relationships between variables cannot be interpreted as causal. In addition, the study population that was examined in the present report may not have been representative of the overall Chinese children population. Last, although we had information on several indicators of socioeconomic position, some of which we did not include in the final model, we cannot rule out the possibility of residual confounding.

Thus, the association between anthropometric indices and childhood hypertension, diagnostic indices should take into account. Serological indicator such as low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) should be further study.

Public health implication

The study explored the discriminating power of integrated covariates for childhood hypertension in Chinese. Our results support the needs for childhood hypertension intervention. Integrated covariates is easy and cheap to measure, So integrated covariates can be served as a standard screening tool for better comparisons of epidemiological data between different studies.

Conclusion

Obesity index, including body mass index and waistline, etc, is not only an important evaluation indicator of children obesity, but also have influence on the prevalence of childhood hypertension. Thus, a simple and effective anthropometric index to identify childhood hypertension in the early period has great significance to improve and promote children health.

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Conflict of interest

Authors declare that they have no conflict of interest.

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Original / *Obesidad*

Fórmula CUN-BAE y factores bioquímicos como marcadores predictivos de obesidad y enfermedad cardiovascular en pacientes pre y post gastrectomía vertical

Lorea Zubiaga Toro, Jaime Ruiz-Tovar Polo, María Díez-Tabernilla, Lorena Giner Bernal, Antonio Arroyo Sebastián y Rafael Calpena Rico

Servicio de Cirugía General y del Aparato Digestivo. Unidad de Cirugía Bariátrica y Metabólica. Hospital General Universitario de Elche. Elche. España.

Resumen

Introducción: El Índice de Masa Corporal (IMC) es uno de los parámetros más utilizados en cirugía bariátrica. Sin embargo, no discrimina el peso asociado a adiposidad. La fórmula CUN-BAE es una ecuación que permite calcular el Porcentaje de Grasa Corporal (PGC) o adiposidad, basándose en valores fáciles de disponer (edad, sexo e IMC). Con esta nueva clasificación muchos de los sujetos considerados con normopeso o sobrepeso ($IMC \leq 30 \text{ kg/m}^2$) en realidad tienen un PGC alto y presentan comorbilidades asociadas a la obesidad. El objetivo de este estudio es evaluar PGC cuantificado mediante fórmula CUN-BAE como marcador predictivo de riesgo cardiovascular en pacientes obesos mórbidos, antes y después de ser sometidos a Gastrectomía Vertical (GV).

Material y métodos: Realizamos un estudio observacional retrospectivo de mujeres intervenidas de GV entre 2007 y 2012 en el Hospital General Universitario de Elche, calculando el PGC mediante la fórmula CUN-BAE de forma preoperatoria y 12 meses tras la intervención. Se correlacionaron estos valores con diferentes parámetros metabólicos y de riesgo cardiovascular.

Resultados: Se estudiaron 50 mujeres. Preoperatoriamente, el IMC medio de $50,4 \pm 7,4 \text{ kg/m}^2$ y PGC del $54,8 \pm 3\%$. Al año de la intervención, el IMC medio era de $27,7 \pm 2,6$ y el PGC $39,4 \pm 3,7\%$. La PGC se correlacionó significativamente con 3 factores bioquímicos asociados con mayor riesgo cardiovascular (cortisol, vitamina D y cociente TG/HDL).

Conclusión: la adiposidad, según la fórmula CUN-BAE, y el análisis de factores bioquímicos predictivos de obesidad, de forma conjunta suponen herramientas útiles para valorar el riesgo de enfermedad cardiovascular, después de GV.

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Palabras clave: Cirugía bariátrica. Índice de Masa Corporal. Fórmula CUN-BAE. Factores de riesgo cardiometabólico.

Correspondencia: Lorea Zubiaga Toro.
Servicio de Cirugía General y del Aparato Digestivo.
Unidad de Cirugía Bariátrica y Metabólica.
Hospital General Universitario de Elche.
Camí de L'Almassera, 11.
03203 Elche. Alicante. España.
E-mail: loreazubiaga@gmail.com

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CUN-BAE FORMULA AND BIOCHEMICAL FACTORS AS PREDICTIVE MARKERS OF OBESITY AND CARDIOVASCULAR DISEASE IN PATIENTS BEFORE AND AFTER SLEEVE GASTRECTOMY

Abstract

Introduction: Body Mass Index (BMI) is one of the most used parameters in bariatric surgery. However, it does not discriminate the weight associated with adiposity. CUN-BAE formula is an equation that calculates Body Fat Percentage or adiposity, based on easily available values (age, sex and BMI). With this new classification many of the subjects that was considered normal weight or overweight ($BMI \leq 30 \text{ kg/m}^2$) really have a higher adiposity and they have comorbidities associated with obesity. The objective of this study is to evaluate the adiposity by formula CUN-BAE as a predictive marker of cardiovascular risk in morbidly obese patients before and after sleeve gastrectomy.

Material and methods: We performed a retrospective observational study of women that were intervened with sleeve gastrectomy, between 2007 and 2012 at the University General Hospital of Elche. The adiposity was calculated by formula CUN-BAE preoperatively and 12 months after surgery. These values were correlated with different metabolic and cardiovascular risk parameters.

Results: 50 women were studied. Preoperatively, the mean BMI was $50.4 \pm 7 \text{ kg/m}^2$ and adiposity $54.8 \pm 3\%$. One year after surgery, the mean BMI was 27.7 ± 3 and adiposity $39.4 \pm 4\%$. The adiposity was significantly correlated with 3 biochemical factors associated with increased cardiovascular risk (cortisol, vitamin D and ratio TG/HDL).

Conclusion: Adiposity, according to the formula CUN-BAE, and biochemical analysis of predictive factors of obesity together represent useful tools for assessing the risk of cardiovascular disease after sleeve gastrectomy.

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Key words: Bariatric surgery. Body Mass Index. CUN-BAE formula. Cardiometabolic risk factors.

Introducción

El aumento de la incidencia y prevalencia de la obesidad y sus comorbilidades es un importante problema de salud pública. Sorprendentemente, siendo la obesidad una enfermedad crónica, su diagnóstico y tratamiento se descuida con frecuencia, y no se piensa en ella como una condición potencialmente mortal^{2,3}. La obesidad en sí misma es un factor de riesgo para la salud de la población, influyendo en el desarrollo y progresión de diversas enfermedades, como eventos isquémicos cardiovasculares, hipertensión arterial, diabetes mellitus tipo 2, dislipemias, síndrome de apnea-hipopnea del sueño, artropatías y aumenta el riesgo de padecer ciertos tipos de cáncer. Además empeora la calidad de vida del enfermo, limita su actividad diaria, genera problemas psico-sociales y reduce considerablemente la expectativa de vida⁴.

En el siglo XIX, el matemático y estadístico, Adolphe Quetelet, observó que el peso relativo del hombre medio era proporcional al cuadrado de la altura¹. La relación entre el peso corporal medido en kilogramos dividido por el cuadrado de la altura medida en metros pasó a denominarse el Índice de Quetelet y más tarde el Índice de Masa Corporal (IMC)². Los puntos de corte en el IMC son muy útiles en estudios epidemiológicos pero a pesar de su amplio uso, el IMC valora el peso corporal y no proporciona una medida precisa de la composición del organismo. Por lo que con frecuencia este cálculo subestima a personas que, en realidad son obesos. Basándose en los resultados obtenidos del estudio de más de 6.000 sujetos, investigadores de la Clínica Universitaria de Navarra⁴ han desarrollado una nueva ecuación, que permite calcular el Porcentaje de Grasa Corporal (PGC) o adiposidad, sin depender de sofisticada tecnología, basándose en valores fáciles de disponer^{14,15}. La nueva fórmula, denominada CUN-BAE (Clínica Universidad de Navarra-Body Adiposity Estimator) aporta una estimación de la composición de grasa de cada individuo y lo clasifica de acuerdo a rangos previamente establecidos (tabla I).

Con esta nueva clasificación, el grupo de la Clínica Universitaria de Navarra ha demostrado que sujetos considerados delgados o con sobrepeso (IMC menor de 30 kg/m²) en realidad tienen un PGC elevado, lo que podría explicar la manifestación de ciertas comorbilidades, tales como hipertensión, hiperglucemia, hiperinsulinismo, dislipemia y elevación de marcadores de inflamación¹⁴⁻¹⁶.

El objetivo del presente estudio es evaluar la fórmula CUN-BAE como marcador predictivo de factor de riesgo cardiovascular en pacientes obesos mórbidos, antes y después de ser sometidos a gastrectomía vertical (GV).

Material y métodos

Realizamos un estudio observacional retrospectivo de todas las mujeres intervenidas de GV entre 2007 y

Tabla I
Fórmula CUN-BAE (Clínica Universitaria de Navarra-Body Adiposity Estimator)⁴

Fórmula original^a:

Edad	años
Sexo	Varon = 0; Mujer = 1
Altura	metros
Peso	kilogramos
IMC	kg/m ²
	% de adiposidad

De la anterior fórmula se obtiene un porcentaje que luego se ordena según los siguientes rangos^b:

Adiposidad	Masculina	Femenina
Normal	< 20%	< 30%
Sobrepeso	20-25%	30-35%
Obesidad	> 25%	> 35%

^aExisten calculadoras en internet que hacen el procedimiento automático. Ejemplo: www.onlinetrainer.es/CUN-BAE.php

^bRangos calculados en relación a la población caucásica.

2012 en el Hospital General Universitario de Elche, calculando el PGC mediante la fórmula CUN-BAE de forma preoperatoria y 12 meses tras la intervención.

Evaluación preoperatoria

Todos los pacientes fueron evaluados por un equipo multidisciplinar compuesto por cirujanos, endocrinólogos, anestesiistas, endoscopistas, psiquiatras, psicólogos y enfermeras especialistas en nutrición. Las pruebas diagnósticas realizadas incluían ecografía abdominal, endoscopia digestiva alta, pruebas funcionales respiratorias y analítica sanguínea completa con perfil nutricional. Los psiquiatras y psicólogos realizaron entrevistas individuales de los candidatos a cirugía bariátrica para evaluar su implicación en la adherencia a una dieta postoperatoria. Se pautó y explicó por personal de enfermería entrenado una dieta de 1.200 kcal/día, con características de dieta mediterránea, similar a la que deberían seguir tras la cirugía. Una pérdida de peso de al menos un 10% del exceso de peso fue considerada un requisito indispensable para ser seleccionado como candidato a GV. Pacientes con evidencia de reflujo gastroesofágico o aquellos que no alcanzaron la pérdida de peso requerida (reflejo de mala adherencia a la dieta), fueron excluidos del estudio.

Aproximadamente 15 días antes de la intervención, las pacientes se someten a una dieta de pérdida acelerada de peso con una dieta-fórmula hiperprotéica y normocalórica en bricks de 200 kcal cada 6 horas. En el contexto de la cirugía bariátrica, la indicación de dietas altas en proteínas son útiles, ya que conllevan a una pérdida de peso rápida, sin compromiso del tejido magro y la reserva protéica tan necesaria para la rege-

neración de los tejidos. Así mismo estas fórmulas proveen un adecuado nivel de saciedad y diversos estudios avalan que estos sustitutos alimentarios contribuyen a reducir complicaciones intra y post-operatorias¹³.

Técnica quirúrgica

En las pacientes del estudio, todas las intervenciones se realizaron por vía laparoscópica. La principal variante a la técnica habitual de la GV, fue la utilización de sonda de Fouché de 50 Fr para calibrar la manga.

Curso postoperatorio

A las 24 horas tras la intervención se administró al paciente una ampolla de azul de metileno diluida en 200 ml de agua por vía oral para confirmar estanqueidad de la línea de sutura. Posteriormente la paciente comenzaba a tomar agua o infusiones. Al segundo día postoperatorio retomaba los suplementos hiperprotéicos líquidos. Al 3º día postoperatorio el paciente era dado de alta si no había habido incidencias durante el postoperatorio.

Seguimiento

La tasa de seguimiento fue del 100%. Todos los pacientes fueron seguidos al mes, 3, 6, 12, 18 y 24 meses tras la operación. Se registraron la pérdida de peso y la evolución de las comorbilidades. El tratamiento farmacológico fue ajustado en función de las necesidades de cada paciente. Se prescribieron multivitamínicos e inhibidor de bomba de protones, en los casos que lo requirieron. Se recomendó la realización diaria de al menos una hora de ejercicio físico moderado.

Variables

Se registró la pérdida de peso y el Porcentaje de Exceso de Peso perdido (PEP) preoperatorio y postoperatorio a los 12 meses de la cirugía. Se calculó el PGC mediante la fórmula CUN-BAE de forma preoperatoria y 12 meses tras la intervención. Se evaluaron parámetros analíticos, incluyendo perfiles glucémico y lipídico, vitamina D, cortisol sérico y proteína C reactiva (PCR). El riesgo cardiovascular se cuantificó mediante el cociente Triglicéridos/HDL-colesterol.

Análisis estadístico

Todos los análisis estadísticos fueron realizados con el programa SPSS 17.0 (SPSS Inc., Chicago, IL). Las variables cuantitativas que seguían una distribución

normal fueron definidas por media y desviación típica; en las variables no gaussianas se emplearon la mediana y el rango. Las variables cualitativas fueron definidas por número de casos y porcentaje. La comparación entre variables pre y postoperatorias se realizó con el test T de Student para datos pareados (Wilcoxon para variables no gaussianas). Las variables cuantitativas se correlacionaron con el test de Pearson para variables cuantitativas con distribución gaussiana y Spearman para variables no gaussianas. Se consideraron significativos valores de $p < 0,005$.

Resultados

Se incluyeron 50 mujeres con una edad media de $42,7 \pm 10$ años e IMC medio de $50,4 \pm 7$ kg/m². Entre las comorbilidades más frecuentes entre las pacientes se describió: hipertensión arterial, diabetes mellitus 2 (algunas con tratamiento oral y otras con tratamiento insulínico), dislipemias (principalmente hipertrigliceridemia), SAOS con indicación de CPAP, esteatosis hepática, osteoartropatías, etc.

La pérdida de peso preoperatoria fue de $10,2 \pm 4$ kg con un PEP medio del 13%.

Al año de la intervención, la pérdida de peso fue de $45,8 \pm 12$ kg, obteniendo un IMC medio de $27,7 \pm 3$ kg/m² y un PEP medio del 84%.

La tasa de resolución de la diabetes mellitus fue del 84% y de la hipertensión del 87%. La hipertrigliceridemia, la osteoartritis y el SAOS mejoraron en todos los casos, suspendiendo la medicación y la CPAP en el 100% de las pacientes. La hipercolesterolemia mostró una leve mejoría, pero la medicación hipolipemiente no pudo ser suspendida en ningún caso.

Los valores de los resultados pre y postoperatorios vienen reflejados en la tabla II.

Análisis de resultados

Adiposidad y pérdida de peso

Preoperatoriamente el grado de adiposidad según fórmula CUN-BAE clasifica a todos los pacientes como obesos. No obstante, después de GV y a pesar de la pérdida de peso, la adiposidad media persiste elevada. (> 35%) Sólo el 14% de las pacientes presentan valores de adiposidad dentro del rango de sobrepeso, mientras que el resto presentan valores de obesidad. Sin embargo, considerando los valores de referencia del IMC, sólo el 8% de las pacientes estaban dentro del rango de obesidad (IMC 30-35 kg/m²), mientras que el 84% se encontraban en rango de sobrepeso (IMC 25-30 kg/m²) y un 8% dentro del límite de normopeso (IMC < 25 kg/m²). Existe una correlación directa moderada entre el IMC y la adiposidad preoperatoria (Pearson 0,486; $p = 0,004$), lo que aumenta en el postoperatorio (Pearson 0,857; $p < 0,001$).

Tabla II
Resultados de las principales variables medidas en el pre y post-operatorio de gastrectomía vertical

Fase	Preoperatorio	Postoperatorio
Peso (kg)	126,3 ± 22,3 (94,8-194,2)	72,1 ± 9,4 (54,8-90)
IMC (kg/m ²)	50,4 ± 7,4 (38,9-67,2)	27,7 ± 2,6 (22,9-31,7)
Glucosa (mg/dl)	104,3 ± 29,7	81,6 ± 8,3
Triglicéridos (mg/dl)	151,1 ± 56,2	93,2 ± 28,6
Colesterol total (mg/dl)	297,5 ± 48,2	204 ± 45
HDL (mg/dl)	49,2 ± 14,8	66,5 ± 17,2
LDL (mg/dl)	130 ± 49,5	120,1 ± 30,5
Vitamina D	20,4 ± 14,6	38,3 ± 15,6
Cortisol (µg/dl)	37,7 ± 14,9	13,7 ± 5,3
PCR (mg/l)	10,4 (5-43)	5 (2-30)
TG/HDL	4,2 ± 1,9	1,6 ± 0,9
Adiposidad (%)	54,8 ± 3	39,4 ± 3,7

Asociación de la adiposidad con el índice de riesgo cardiovascular

El índice de riesgo cardiovascular (cociente Triglicéridos/HDL-colesterol) muestra un descenso significativo a los 12 meses de la cirugía (desde $4,2 \pm 2$ preoperatorio hasta $1,6 \pm 1$ a los 12 meses; $p < 0,001$). El riesgo cardiovascular preoperatorio se correlaciona con el porcentaje de adiposidad (Pearson 0,517; $p = 0,049$), pero no con el IMC. Lo mismo ocurre en la determinación a los 12 meses de la intervención, correlacionándose con la adiposidad (Pearson 0,776; $p = 0,032$), pero no con el IMC.

Asociación de la adiposidad con otros parámetros analíticos

Los valores de cortisol en el preoperatorio eran de $37,7 \pm 15$ y al año después de la cirugía de $13,7 \pm 5$ ($p = 0,009$). Aunque ni los valores preoperatorios ni los postoperatorios se correlacionan con el IMC ni el porcentaje de adiposidad, el descenso de los niveles séricos de cortisol sí muestra una correlación directa con el descenso de la adiposidad (Pearson 0,463; $p = 0,011$).

Los valores de vitamina D muestran un ascenso tras la intervención (en el preoperatorio eran de $20,4 \pm 15$ y al año después de la cirugía aumentan a $38,3 \pm 15$; $p < 0,001$). Este incremento se correlaciona de forma inversa con el descenso de la adiposidad (Pearson -0,425; $p = 0,033$).

Discusión

El Índice de masa corporal (IMC) es el parámetro más utilizado como herramienta en el diagnóstico actual de la obesidad, pues tiene la ventaja de que la altura de un sujeto y el peso son fáciles y baratos de medir³⁻⁵. La Organización Mundial de la Salud define valores por encima de 30 kg/m^2 como obesidad⁶. Los puntos de corte en el IMC son muy útiles en estudios epidemiológicos⁷ pero a pesar de su amplio uso, el IMC es sólo una medida orientativa y no proporciona una medida de la composición del organismo^{8,9}.

La fórmula CUN-BAE muestra que frecuentemente muchos pacientes son catalogados como “no obesos” según su IMC, en realidad tienen un alto índice de adiposidad. Además, muchos, siendo “delgados” presentan hipertensión, hiperglicemia, hipertrigliceridemia, hiperinsulinemia y aumento de concentraciones de lipoproteínas de baja densidad, fibrinógeno y PCR. Así que el estudio de la Clínica de Navarra define ayuda a entender el riesgo cardiovascular en sujetos con normopeso. Junto a este estudio existen otros trabajos que analizan el impacto del PGC sobre el riesgo cardiometabólico, demostrando que la simple medición del IMC asociado o no al valor de la circunferencia abdominal o cualquier medida antropométrica, es menos eficaz^{10,11}. Sin embargo, los recursos existentes hoy en día para calcular el PGC (impedancia bioeléctrica, peso hidrostático, pletismografía de desplazamiento de aire, absorciometría de rayos X de doble energía, etc.) o bien no están al alcance de todos los medios, o arrojan mediciones estimadas y en la mayoría de los casos, suponen costes elevados para el sistema sanitario público^{12,13}.

Vale destacar que la fórmula CUN-BAE expone que aproximadamente un tercio de las personas clasificadas como delgadas mediante la medición del IMC, tienen en realidad un PGC elevado^{14,15}. Este trabajo evaluó el grado de error en el diagnóstico de obesidad que ofrece el cálculo del IMC. Así pues, concluye que un 29% de las personas que según el IMC se sitúan en el rango de normalidad ofrecen realmente un PGC propio de una persona obesa y que un 80% de las personas que presentan sobrepeso, realmente son obesas^{14,16}.

Por tanto, el IMC realmente no llega a definir el grado de obesidad como el exceso de adiposidad, sino lo que realmente define es un exceso de peso, sin discriminar entre tejido magro, agua o grasa. Estos datos también se muestran en nuestro estudio, donde al año postoperatorio, según el IMC el 84% de las pacientes estaba en rango de sobrepeso y un 8% en normopeso. Pero según fórmula CUN-BAE, el 86% continuaban en rango de obesidad. Esta ausencia de concordancia resulta muy significativa. A pesar de que IMC y adiposidad muestran cierto grado de correlación, ésta es sólo moderada en las mediciones preoperatorios y aumenta ligeramente en las determinaciones postoperatorias.

Al evaluar exclusivamente el número resultante de aplicar la fórmula CUN-BAE en la muestra de pacientes de nuestro estudio, en inicio se observa que éstas continúan siendo obesas (> 35%) después de la cirugía. De allí que quisimos analizar ciertos parámetros bioquímicos y el índice de riesgo cardiovascular (Triglicéridos/HDL-colesterol).

La efectividad de la cirugía no se limita a la disminución de la adiposidad en el organismo, sino que disminuyendo dicha adiposidad se reducen también el riesgo de padecer un evento cardiovascular.¹⁷ En nuestro medio, hay dos predictores de riesgo cardiovascular ampliamente utilizados: la relación Triglicéridos/HDL-colesterol (TG/HDL) y la puntuación de riesgo de Framingham, que analiza la edad, sexo, colesterol total, HDL-colesterol, tabaco hábito y la presión arterial sistólica. Se considera que la escala de Framingham es una fórmula más ajustada a la situación real para determinar el riesgo cardíaco¹⁷, no obstante su aplicación es más compleja. Debido a esto, se prefiere el uso de la TG/HDL, que puede cuantificarse numéricamente y no se expresa como una probabilidad de ocurrencia de evento cardíaco. En diversos informes señalan que un índice TG/HDL superior a 3 se asocia a riesgo cardiovascular. En nuestro estudio este índice se ve reducido de su valor preoperatorio medio de 4,2 a un valor postoperatorio al año de 1,6 ($p < 0,001$). El hecho de que este índice de riesgo cardiovascular se correlacione con el porcentaje de adiposidad, tanto preoperatorio como al año postoperatorio, pero no con el IMC, indica que el valor obtenido de la fórmula CUN-BAE es un mejor reflejo del riesgo cardiovascular, que el IMC. A pesar de que el valor medio de adiposidad a los 12 meses de la intervención se encuentre aún en el rango de obesidad, hemos observado un descenso muy significativo del mismo desde los valores de partida. Además, este valor postoperatorio de adiposidad se correlaciona con el índice de riesgo cardiovascular, que a su vez se encuentra dentro del rango de la normalidad. Todo ello hace pensar, que a pesar de que los valores de PCG continúan elevados el riesgo cardiovascular se consigue normalizar, lo que en definitiva es el objetivo principal de la cirugía bariátrica, y no la simple pérdida de peso.

Adiposidad y cortisol:

El cortisol parece desempeñar un papel en la adiposidad ya que las concentraciones circulantes de cortisol son más altas en las personas con obesidad, con o sin síndrome metabólico, que en personas sanas. También está bien documentado que el cortisol promueve la diferenciación y proliferación de adipocitos humanos y sus receptores son más abundantes el tejido adiposo visceral que en el subcutáneo¹⁸. Además, también contribuye a redistribuir la grasa periférica a depósitos centrales, a la activación de la lipólisis y a la liberación de ácidos gra-

dos libres en la circulación, aumentando el riesgo de aterosclerosis y finalmente el riesgo de enfermedad cardiovascular. Como ya hemos mencionado, la pérdida de peso reduce el riesgo cardiovascular en pacientes obesos. De la misma manera, la pérdida de peso tiende a normalizar los niveles de cortisol. De acuerdo con esto, los niveles de cortisol podrían ser considerados como reflejo del riesgo cardiovascular. En nuestro estudio hemos observado que el descenso de la adiposidad se correlaciona de forma directa con el descenso en los valores de cortisol. Un estudio previo de nuestro grupo demostró que a partir del 6º mes el descenso de la cortisolemia se correlacionaba con un descenso en el riesgo cardiovascular^{17,18}. Todo ello confirma que la adiposidad es un buen predictor del riesgo cardiovascular.

Adiposidad y vitamina D

En los últimos años, se han descubierto acciones de la vitamina D distintas de las que atañen al metabolismo de los huesos, lo que se ha denominado acciones no calcémicas. Estos hallazgos vienen a demostrar que esta vitamina es un compuesto con múltiples funciones, que hacen pensar en ella en una hormona más que en una vitamina inerte^{19,20}. La carencia de vitamina D en los pacientes obesos se sigue asociando al déficit metabólico y a la alteración en los niveles de lípidos (colesterol y triglicéridos), lo cual hace pensar que es un factor modificable que al corregirlo, puede influir de manera beneficiosa en el riesgo vascular de estos pacientes¹⁹. La vitamina D se almacena en gran medida en el tejido adiposo de los pacientes obesos, lo que puede llegar a originar un hiperparatiroidismo secundario. Según se va perdiendo peso, los valores séricos de vitamina D van aumentando. Esto explica la correlación inversa entre el descenso de la adiposidad y el aumento de los valores de vitamina D en el plasma de nuestras pacientes²⁰.

Conclusión

La adiposidad, según la fórmula CUN-BAE, es un mejor predictor del riesgo cardiovascular que el IMC. El PCG si bien no reduce a porcentajes normales, sí disminuye el riesgo cardiovascular. El descenso del cortisol y el aumento de la vitamina D se asocian con el descenso de la adiposidad y, por tanto, pueden ser herramientas útiles para valorar la disminución del riesgo de enfermedad cardiovascular, después de cirugía bariátrica.

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Original / *Obesidad*

Estudio longitudinal del peso e índice de masa corporal tras el trasplante renal durante 5 años de evolución

Rafael Fernández Castillo¹, Ruth Fernandez Gallegos², Rafael José Esteban de la Rosa² y María Pilar Peña Amaro³

¹Universidad de Granada. Facultad de Ciencias de la Salud. Departamento de Enfermería. ²Servicio de Nefrología Unidad de Hemodiálisis. Hospital Universitario Virgen de las Nieves. Granada. ³Universidad de Jaén. Facultad de Ciencias de la Salud. Departamento Enfermería. Jaén. España.

Resumen

Introducción: El aumento de peso después del trasplante es relativamente común, además suele ser multifactorial y suele estar influenciado por glucocorticoides y los medicamentos inmunosupresores, pudiendo retrasar la función del injerto y provocar complicaciones graves de salud.

Objetivos: Evaluar los cambios en el peso, grado de obesidad e índice de masa corporal así como el efecto que el tratamiento inmunosupresor produce sobre estos 5 años postrasplante renal sobre estos.

Métodos: La muestra estuvo formada por 119 pacientes trasplantados renales, 70 hombres y 49 mujeres, trasplantados renales, que asistieron durante cinco años a la consulta postrasplante. A todos los pacientes se realizaron mediciones pretrasplante y postrasplante (desde el 1º año hasta el 5º año) de peso, altura e índice de masa corporal calculado mediante la fórmula peso/talla² relacionándolo con el tratamiento inmunosupresor que tomaban.

Resultados: Existe un aumento considerable del índice de masa corporal, peso y grado de obesidad en el primer año tras el trasplante aumentando mas lentamente en los siguientes cuatro años. El tipo de tratamiento inmunosupresor influencia el peso y grado de obesidad que se produce en este periodo de tiempo.

Conclusiones: Hay una elevada prevalencia sobrepeso y obesidad tras el trasplante especialmente durante el primer año. Al año los pacientes ganan una media de 6,6 kg de peso y una media de 2,5 kg/m² en su IMC. Durante el tratamiento se debe minimizar las dosis de esteroides e incluir tratamiento dietético y ejercicio físico adecuado.

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Palabras clave: Trasplante renal. Obesidad. Grado de obesidad. Antropometría. Índice de masa corporal.

Correspondencia: Rafael Fernández Castillo.
Universidad de Granada.
Facultad de Ciencias de la Salud. Campus de Ceuta.
C/ Cortadura del Valle, s/n.
51001 Ceuta. España.
E-mail: rafaelfernandez@ugr.es

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LONGITUDINAL STUDY OF WEIGHT AND BODY MASS INDEX AFTER RENAL TRANSPLANTATION DURING 5 YEARS OF EVOLUTION

Abstract

Introduction: Gain weight after transplantation is relatively common, also tends to be multifactorial and can be influenced by glucocorticoids and immunosuppressive medications, delayed graft function and cause serious health complications.

Objectives: Assess changes in weight, degree of obesity and body mass index as well as the effect of immunosuppressive treatment over these 5 years after kidney transplantation.

Methods: The samples were 119 kidney transplant recipients, 70 men and 49 women, that attended the query post for five years. All patients were measured Pretransplant and post (from 1st year to the 5th year) weight, height and body mass index calculated by the formula weight/size² relating it to immunosuppressive treatment taking.

Results: There is a considerable increase of body mass index, weight and degree of obesity in the first year after transplantation to increase more slowly in the next four years. The type of immunosuppressive treatment influence the weight and degree of obesity that occurs in this period of time.

Conclusions: A high prevalence there are overweight and obesity after the transplant especially during the first year. A year patients earn an average of 6.6 kg in weight and an average of 2.5 kg/m² in their BMI. During treatment should minimize doses of steroids and include dietary treatment and adequate physical exercise.

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Key words: Kidney transplantation. Obesity. Obesity degree. Anthropometry. Body mass index.

Introducción

El aumento de peso después del trasplante renal es frecuente y el sobrepeso y la obesidad resultante se asocia con complicaciones graves de salud.

Actualmente la causa de aumento de peso entre la población general adulta es multifactorial y puede estar influenciada por varios factores como: la herencia genética, el sexo, la edad, la raza, la alimentación, el estilo de vida, estado de salud etc. Estas mismos factores son válidas para los pacientes trasplantados renales, en los que se ha observado una tendencia hacia el aumento excesivo de peso después del trasplante. No obstante, los receptores de trasplante renal también deben combatir los factores específicos de su población, es decir, los efectos provocados por glucocorticoides y los medicamentos inmunosupresores en el aumento de la grasa corporal acumulación y retención de líquido^{1,2}.

Los esteroides son conocidos por mejorar el apetito y para tener un efecto adverso sobre la distribución de la grasa corporal y el metabolismo de lípidos contribuyendo así al patrón de ganancia de peso observada después del trasplante^{3,4}. Sin embargo, otros factores, como una mayor sensación de bienestar, pueden desempeñar un papel igualmente importante. Entre los receptores de trasplante renal, hay evidencia de que el aumento de peso de más del 10 %, aumenta las posibilidades de padecer diabetes y dislipemia inducida por esteroides^{5,6}. Además, tienen una mayor prevalencia de hipertensión arterial, enfermedad arterial coronaria, enfermedad pulmonar obstructiva crónica y enfermedad vascular periférica, accidente cerebrovascular, arteriosclerosis y mortalidad⁷. Así mismo hay una fuerte evidencia de que la obesidad afecta negativamente a la función y la supervivencia del injerto tanto a corto como a largo plazo. En la población general, por lo que las intervenciones dietéticas juegan un papel central en el control del sobrepeso y la obesidad⁸.

En este estudio retrospectivo, se evaluaron los cambios en el peso e Índice de Masa corporal así como el efecto que el tratamiento inmunosupresor produce sobre estos 5 años posttrasplante renal sobre estos.

Material y métodos

Sujetos

La muestra estuvo formada por 119 pacientes trasplantados renales de ambos sexos que acuden de forma periódica a la consulta de Trasplante Renal en el Hospital Universitario Virgen de las Nieves de Granada. No fueron seleccionados mediante procedimientos de muestreo aleatorio y su participación en el estudio viene determinada por la asistencia a la consulta para su seguimiento y control. Las edades estaban comprendidas entre 18 y 74 años, 70 hombres y 49 mujeres que fueron seguidos durante 5 años.

Métodos

El protocolo inmunosupresor consistió en: (Est) Esteroides asociados con (MMF) Micofenolato mofetilo mas (Tac) Tacrolimus y CD25, (Csa) Ciclosporina y (TMG) Timoglobulina. La dosis de prednisona durante las primeras 4 semanas fue de 20 mg/día, en dosis única matutina, con reducción progresiva hasta establecer dosis de 5-10 mg/día al mes 3°. La dosis de CsA, dividida en dos, se ajustó para obtener niveles valle entre 150-250 ng/mL en los primeros 6 meses de trasplante y posteriormente entre 100-150 ng/mL. La dosis de Tacrolimus, dividida en dos, fue ajustada para mantener niveles de 10-15 ng/mL en los primeros 3 meses tras el trasplante, y posteriormente entre 5-8 ng/ml. La dosis de MMF, repartida en dos dosis, osciló entre 1-2 g/día. En total se investigaron 4 grupos de inmunosupresores asociados: Grupo 1: Est+MMF+Tac+CD25, Grupo 2: Est+MMF+CsA+CD25, Grupo 3 Est+MMF+Tac+TMG, Grupo 4: Est+MMF+Tac.

Además se les efectuaron mediciones antropométricas de peso y altura a los 6, 12, 24, 36, 48 y 60 meses. El peso se midió por una balanza tallímetro Perperson 113.481 en kilogramos y la altura en centímetros. El índice de masa corporal fue calculado mediante la fórmula: peso/talla² (kg)/(m)² y agrupada según la clasificación de la OMS en IMC < 18,50 infrapeso, 18,50 a 24,99 normal, 25 a 26,9 sobrepeso grado I, 27 a 29,9 sobrepeso grado II, 30 a 34,9 obesidad Tipo I, 35 a 39,9 obesidad tipo II, Obesidad tipo III Mórbida 40 a 49,9.

A todos los pacientes se les se les recomendó antes del alta del hospital consumir 1.4 a 1.5 g/kg por día de proteína dieta de 30 a 35 calorías (kcal)/kg/día durante los primeros 3 meses después del trasplante renal así mismo los lípidos no debían representar más del 30% de la ingesta total de la dieta evitando el consumo de azúcares simples. Después de 3 meses, se les recomienda a los pacientes reducir el consumo de proteínas a 1 g/kg por día.

Análisis estadístico

El análisis se realizó mediante el paquete estadístico IBM SPSS Statics 20, Los resultados se expresan como frecuencias, porcentajes y media $\pm$ desviación estándar para las variables peso, IMC y tratamiento inmunosupresor. Para valorar las diferencias entre peso y sexo de pacientes, se utilizó el análisis de varianza (ANOVA), Todos los datos se expresan en valor medio + desviación estándar ($X \pm DS$), considerándose significación estadística con valores de $p < 0,05$.

Resultados

La edad media en los hombres fue de $56,43 \pm 10,79$ y en las mujeres $54,19 \pm 11,81$. En general, el mayor aumento de peso se produce al año del trasplante man-

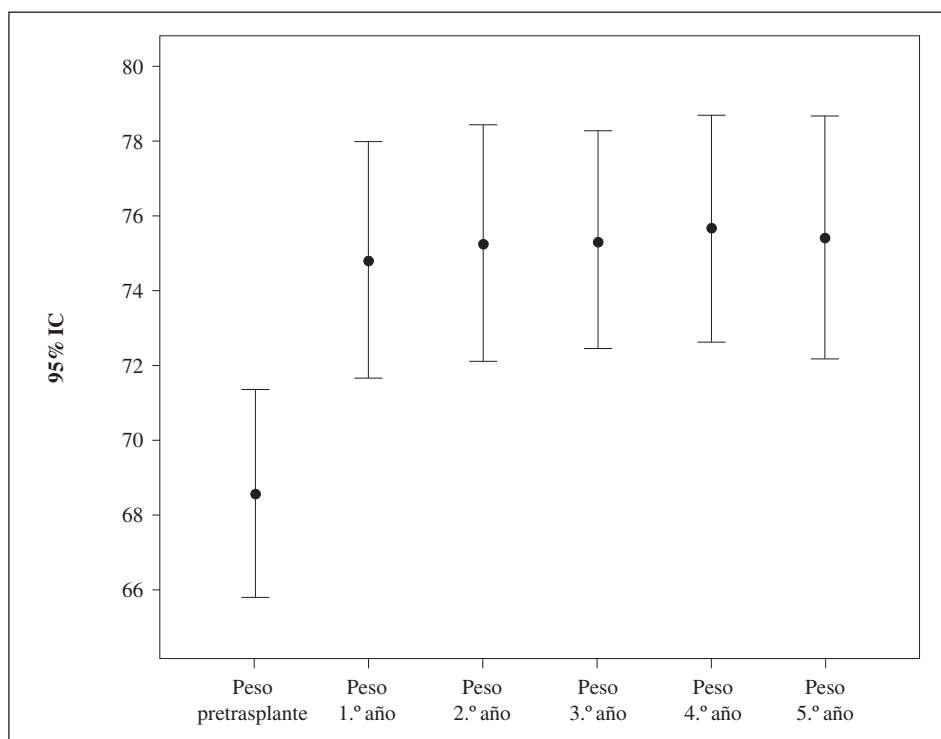


Fig. 1.—Evolución del peso tras el trasplante renal.

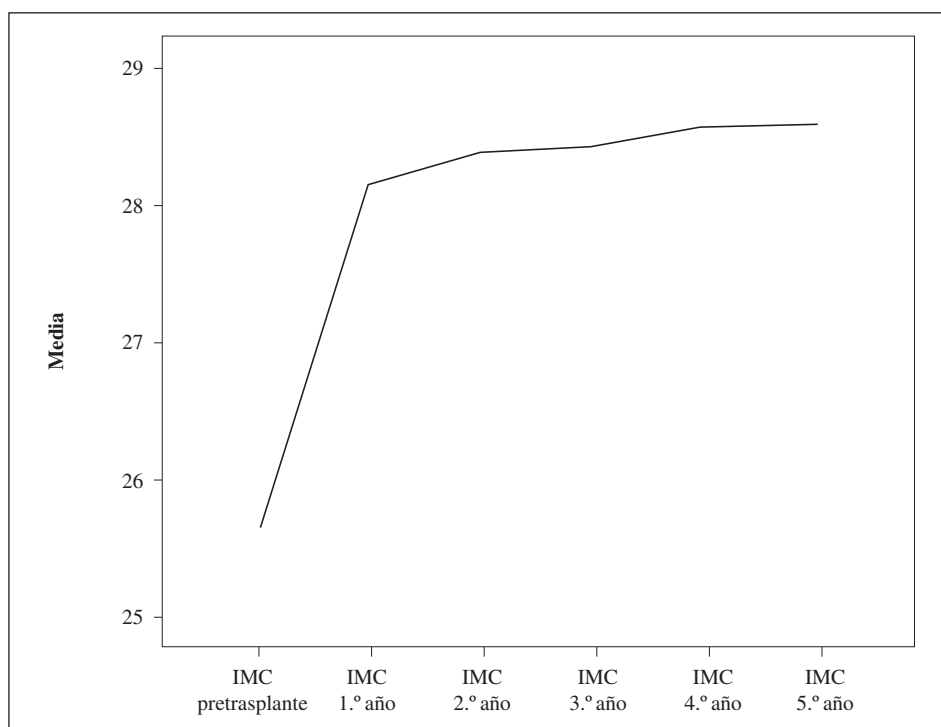


Fig. 2.—Evolución del índice de masa corporal tras el trasplante renal.

teniéndose una tendencia al alza incluso hasta el 5º año (fig. 1), lo mismo sucede con el IMC, el mayor aumento se produce al año del trasplante y la línea es seguir aumentando durante en años sucesivos (fig. 2).

Los hombres presentan mayores pesos que las mujeres en todos los años medidos (Peso pretrasplante F =

8,9; Peso 1º año F = 7,5; Peso 2º año F = 9,1; Peso 3º año F = 7,6; Peso 4º año F = 4,9; Peso 5º año F = 5,1; ($p < 0,05$). En los hombres se produce un aumento considerable de peso en el primer años tras el trasplante de 5,96 kg y los mismo ocurre en el grupo de las mujeres alcanzando un peso de 5,72 kg, esta tendencia continua

Tabla I
Media de pesos por sexos desde el momento pretrasplante al 5.º año de trasplante

<i>Peso</i>	<i>Sexo</i>	<i>Media</i>	<i>Desviación típica</i>	<i>Mínimo</i>	<i>Máximo</i>
Peso pretrasplante	Hombre	70,99	10,25	50,0	97,0
	Mujer	64,27	13,57	41,0	98,0
Peso 1.º año	Hombre	76,95	11,09	56,8	109,5
	Mujer	69,99	15,01	49,7	112,0
Peso 2.º año	Hombre	77,45	12,33	46,7	107,8
	Mujer	68,80	16,67	13,8	104,0
Peso 3.º año	Hombre	76,99	11,49	48,5	102,0
	Mujer	69,73	13,44	43,2	100,5
Peso 4.º año	Hombre	76,78	11,49	47,0	105,6
	Mujer	70,61	12,80	52,4	105,6
Peso 5.º año	Hombre	78,47	11,32	57,3	106,3
	Mujer	71,21	13,80	51,5	108,0

p < 0,05.

Tabla II
Porcentaje de pacientes con grado de obesidad según la OMS desde el momento pretrasplante al 5.º año de trasplante

<i>Grado de obesidad</i>	<i>Pretrasplante</i>	<i>1.º año</i>	<i>2.º año</i>	<i>3.º año</i>	<i>4.º año</i>	<i>5.º año</i>
Infrapeso IMC < 18,50	1,1%	1%	2,2%	2,3%	2,9%	0%
Normopeso 18,50 a 24,99	47,4%	29,4%	24,7%	21,6%	18,6%	26,7%
Sobrepeso grado I 25 a 26,9	24,2%	15,7%	15,1%	18,2%	21,4%	13,3%
Sobrepeso grado II 27 a 29,9	15,8%	29,4%	23,7%	27,3%	22,9%	21,7%
Obesidad Tipo I 30 a 34,9	8,4%	15,7%	24,7%	22,7%	27,1%	31,7%
Obesidad tipo II 35 a 39,9	2,1%	7,8%	7,5%	5,7%	4,3%	1,7%
Mórbida 40 a 49,9	1,1%	1%	2,2%	2,3%	2,9%	5%

incluso durante los cinco años siguientes alcanzando un peso al quinto año de 7,48 kg para los hombres y de 6,94 kg para las mujeres (tabla I).

Casi todos los pacientes presentaban algún grado de obesidad antes de ser trasplantados, pero casi la mitad presentaban un IMC normal, este dato disminuye durante los siguientes años tras el trasplante ya que aumenta el porcentaje de pacientes con sobrepeso en general, siendo de destacar el considerable aumento en el porcentaje de pacientes con Sobrepeso Tipo I y Tipo III u obesidad mórbida (tabla II).

En cuanto a los tratamientos inmunosupresores todos los grupos producen una elevación del peso desde el primer mes postrasplante al año de aproximadamente 5,5 kg de media, aumentando levemente durante los siguientes años postrasplante para aumentar en 6,8 kg de media al 5º año postrasplante, este hecho es mas destacable sobre todo en el Grupo 3 donde se produce una ganancia de peso en 5 años de 11 kg. y en el Grupo 4 de 8 kg (tabla III).

Discusión

Como podemos observar se produce un importante y elevado aumento del peso y del IMC tras el trasplante renal (figs. 1 y 2), esto representa un grave problema ya que la obesidad tras el trasplante renal es un importante factor de riesgo tanto para la supervivencia del injerto como para el desarrollo de enfermedades cardiovasculares, hipertensión diabetes y dislipemias, y además representa un causa importante de morbilidad y mortalidad en estos pacientes^{9,10}.

Existe una alta prevalencia de pacientes trasplantados que presenta varios grados de obesidad, en nuestro estudio podemos observar que va desde un 70% del primer año postrasplante al 75% del quinto año (tabla II). Esta situación representa un problema importante para la gestión y la labor clínica, dadas las consecuencias potenciales y la posterior dificultad en la consecución de peso normal^{11,12}. Asi mismo tambien podemos observar que se produce una mayor ganancia de peso

Tabla III
Media de pesos por grupos de medicación inmunosupresora

		<i>Media</i>	<i>Desviación típica</i>	<i>Mínimo</i>	<i>Máximo</i>
Peso 1 mes	Grupo 1	68,65	10,64	44,4	94,6
	Grupo 2	73,15	9,98	57,5	98,8
	Grupo 3	71,55	15,57	46,6	96,5
	Grupo 4	66,42	10,59	48,2	89,8
Peso 1 año	Grupo 1	74,48	12,83	50,1	112,0
	Grupo 2	74,96	8,93	58,6	91,0
	Grupo 3	76,48	17,35	49,7	109,5
	Grupo 4	71,52	11,27	53,8	94,5
Peso 2 año	Grupo 1	73,73	15,67	13,8	104,0
	Grupo 2	75,76	8,48	59,0	92,7
	Grupo 3	77,02	18,07	48,5	107,8
	Grupo 4	70,95	12,50	46,7	96,2
Peso 3 año	Grupo 1	73,42	11,48	43,2	94,2
	Grupo 2	77,30	10,25	59,2	95,6
	Grupo 3	76,99	16,19	46,6	102,0
	Grupo 4	71,60	12,64	55,8	100,5
Peso 4 año	Grupo 1	73,73	11,53	47,0	93,0
	Grupo 2	77,24	7,20	68,1	88,2
	Grupo 3	76,88	15,60	56,0	105,6
	Grupo 4	71,77	13,00	56,7	105,6
Peso 5 año	Grupo 1	73,00	11,0	51,5	94,0
	Grupo 2	76,36	8,18	66,1	87,7
	Grupo 3	82,58	15,39	60,9	106,3
	Grupo 4	74,54	14,65	54,5	108,0

Grupo 1: Est+MMF+Tac+CD25, Grupo 2: Est+MMF+CsA+CD25, Grupo 3 Est+MMF+Tac+TMG, Grupo 4: Est+MMf+Tac.

en hombres que en mujeres (tabla I), hecho que no concuerda con otros estos estudios donde se produjo un aumento en la incidencia de peso importante en las mujeres de casi el doble que en los hombres durante un período de 10 años.

En nuestro estudio la ganancia de peso al año fue del 8% y del 11% a los 5 años, hemos encontrado similitudes con otros estudios donde la ganancia de peso a 5 años fue del 10,9% durante el primer año y el 15,3% a los 5 años^{13,14}.

La etiopatogenia de la obesidad en el trasplante renal es multifactorial y muchas de las variables que afectan en el trasplante renal son similares a los que afectan a la población en general (por ejemplo, los factores genéticos y ambientales y el estilo de vida sedentario)¹⁵⁻¹⁸. Otros factores más específicamente relacionados con el trasplante son la resolución del estado urémico, el estado general del paciente, y la terapia inmunosupresora¹⁹⁻²¹. Los efectos de los esteroides son un factor clave para promover la ganancia de peso debido a sus efectos metabólicos, redistribución de grasa corporal, retención de agua, y, en particular, el aumento del apetito^{22,23}, en este estudio se puede observar que los cuatro grupos de inmunosupresores aplicados durante los 5 años contenían dosis de esteroides y todos produjeron un considerable aumento de peso observable durante los 5 años de seguimiento.

Por lo tanto la obesidad tiene un efecto desfavorable en la evolución clínica del trasplantado renal y esta asociada con un retraso en la función y supervivencia del injerto, aumento en la incidencia de complicaciones cardiovasculares, hipertensión, diabetes y dislipidemia, así como con un aumento de las complicaciones quirúrgicas (en especial relacionadas con la herida quirúrgica) y un mayor riesgo de complicaciones urológicas²⁴⁻²⁶.

En el tratamiento de la obesidad el apoyo psicológico dirigido a corregir los hábitos alimenticios también ha demostrado ser útil. Sin embargo, el método más eficaz es la prevención de la obesidad, empezando desde cuando el paciente está en diálisis y continuando inmediatamente tras la realización del trasplante²⁷. El tratamiento farmacológico con inhibidores de las lipasa (Orlistat) está contraindicado, ya que interfiere con la absorción de los inhibidores de la calcineurina²⁸. En cuanto al tratamiento quirúrgico de la obesidad se debe reservar para los pacientes con obesidad mórbida que no responden al tratamiento convencional. Lo ideal es lograr un índice de masa corporal < 25, sin embargo, un objetivo más realista que ha demostrado ser beneficioso en el trasplante es una reducción de 5%-10% del peso corporal durante un período de 6 meses con el consiguiente mantenimiento de pérdida de peso en años sucesivos^{29,30}.

En conclusión, hay una elevada prevalencia sobre peso y obesidad tras el trasplante especialmente

durante el primer año. Al año los pacientes ganan una media de 6,6 kg de peso y una media de 2,5 kg/m² en su IMC. El tratamiento para la obesidad en el trasplante renal debe incluir tratamiento dietético, ejercicio físico adecuado, y la minimización de las dosis de esteroides.

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Original / *Obesidad*

Fiabilidad y validez de la versión mexicana del cuestionario Pro Children Project

Gerardo Ochoa-Meza¹, Juan Carlos Sierra², Carmen Pérez-Rodrigo³, Javier Aranceta Bartrina⁴ y
Óscar A. Esparza-Del Villar¹

¹Departamento de ciencias sociales. Universidad Autónoma de Ciudad Juárez. México. ²Departamento de Personalidad, Evaluación y Tratamiento. Universidad de Granada. España. ³Unidad de Nutrición Comunitaria. Bilbao. España. ⁴Departamento de Ciencias de la Alimentación. Fisiología y Toxicología. Universidad de Navarra. España.

Resumen

Objetivo: Determinar la fiabilidad test-retest, la consistencia interna y la validez predictiva de los constructos de la versión mexicana del cuestionario Pro Children Project (PCHP), que evalúa factores psicosociales personales y ambientales asociados a el consumo de fruta y verdura en niños escolares de 10 a 12 años.

Métodos: Diseño test-retest con un intervalo de 14 días. Una muestra de 957 niños de ocho escuelas primarias completaron el cuestionario de 82 ítems en el 2012 en Ciudad Juárez, Chihuahua, México.

Resultados: La confiabilidad test-retest fue moderada (coeficiente de correlación intraclass (CCI) > 0,60) en todos los constructos de fruta y de verdura en un rango de 0,60 a 0,68. El promedio de valores Alfa de Cronbach fueron de bajos a altos (rango: 0,54 a 0,92), comparables al estudio original. La validez predictiva fue de moderada a buena en un rango de correlaciones de Spearman de 0,23 a 0,60 en factores personales y de 0,14 a 0,40 en factores ambientales.

Conclusión: Los resultados demuestran una fiabilidad y validez suficiente de la versión mexicana del cuestionario PCHP para la evaluación global de factores psicosociales personales y ambientales asociados a el consumo de fruta y verdura en niños escolares de 10 a 12 años. Finalmente, se discuten las implicaciones para la aplicación de este instrumento en contextos escolares y las pautas a seguir para futuras investigaciones.

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Palabras clave: Cuestionario. Reproducibilidad de resultados. Hábitos alimentarios. Niños. México.

RELIABILITY AND VALIDITY OF A MEXICAN VERSION OF THE PRO CHILDREN PROJECT QUESTIONNAIRE

Abstract

Objective: To determine the test-retest reliability, the internal consistency, and the predictive validity of the constructs of the Mexican version of the Pro Children Project questionnaire (PCHP) for assessing personal and environmental factors related to fruit and vegetable intake in 10-12 year-old schoolchildren.

Method: Test-retest design with a 14 days interval. A sample of 957 children completed the questionnaire with 82 items. The study was conducted at eight primary schools in 2012 in Ciudad Juárez, Chihuahua, Mexico.

Results: For all fruit constructs and vegetable constructs, the test-retest reliability was moderate (intra-class correlation coefficient (ICC) > 0.60). Cronbach's alpha values were from moderate to high (range of 0.54 to 0.92) similar to those in the original study. Values for predictive validity ranged from moderate to good with Spearman correlations between 0.23 and 0.60 for personal factors and between 0.14 and 0.40 for environmental factors.

Conclusions: The results of the Mexican version of the PCHP questionnaire provide a sufficient reliability and validity for assessing personal and environmental factors of fruit and vegetable intake in 10-12 year old schoolchildren. Finally, implications to administer this instrument in scholar settings and guidelines for futures studies are discussed.

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Key words: Questionnaire. Reproducibility of results. Foods habits. Child. Mexico.

Correspondencia: Gerardo Ochoa-Meza.
Universidad Autónoma de Ciudad Juárez.
Departamento de Ciencias Sociales.
Av. Universidad y Heroico Colegio Militar s/n.
32310 Ciudad Juárez, Chih. México.
E-mail: gochoaster@gmail.com

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Abreviaturas

CF y V: Consumo de fruta y verdura.
PCHP: Pro Children Project.
CCI: Coeficiente de correlación intraclase.
IC: Intervalo de confianza.
SPSS: Statistical package for the social science.

Introducción

El consumo de fruta y verdura (CF y V) posiblemente juega un papel determinante en los programas de prevención de la obesidad infantil^{1,2}. Algunas evidencias epidemiológicas sugieren que altos niveles de CF y V asociados a actividad física contribuyen a la prevención de padecimientos cardiovasculares, diabetes y ciertos tipos de cáncer³⁻⁵. Sin embargo, ante la epidemia global de obesidad y sobrepeso, el CF y V generalmente es menor a lo recomendado⁶⁻⁸. En México el bajo consumo se ubica en dos o menos piezas por día y el más alto en tres piezas por día, además las tasas actuales de obesidad y sobrepeso constituyen un grave problema de salud pública en niños y adolescentes^{9,10}.

El diseño de intervenciones para elevar los niveles de CF y V en poblaciones escolares requiere de constructos psicosociales, que medien o moderen la conducta nutricional e influyan en la obtención de resultados efectivos^{12,13}. Constructos como la accesibilidad y las preferencias han mostrado una alta consistencia en la promoción de conductas alimentarias saludables¹⁴⁻¹⁶. Es decir, las preferencias desde la perspectiva de la prevención pueden ser una medida clave entre otros constructos que pueden contribuir a la solución de problemas de salud pública¹⁷. Las preferencias son también un predictor o mediador potente de las diferencias de género en el CF y V, sin embargo, el gusto y autoeficacia median parcialmente entre la accesibilidad a la fruta y su consumo^{4,18}. Algunos modelos como el sociocognitivo o el modelo ecológico de conducta saludable pueden explicar y predecir conductas de consumo saludable^{19,20}. Asimismo, ciertos factores de la percepción ambiental social, tales como la accesibilidad, la modelación, las reglas exigidas por la familia y el conocimiento de las recomendaciones acerca del CF y V son importantes para incrementar este consumo^{21,22}. De manera que, para elevar los niveles de consumo se requiere de instrumentos válidos y fiables, que contengan los determinantes o los mediadores más importantes del CF y V, con el fin de mejorar la eficiencia de las intervenciones diseñadas a la medida de las necesidades de las poblaciones escolares.

El “Pro Children Project” ha identificado factores psicosociales dirigidos a incrementar el CF y V en niños escolares europeos y sus padres, determinando las categorías de factores (personales y ambientales) de mayor influencia para el CF y V⁴. Este proyecto desarrolló y validó un cuestionario de autoreporte con base en constructos sustentados tanto en teorías, como en modelos psicosociales y en la promoción de la salud²³. El cuestionario

PCHP identifica factores personales (autoconsumo, conocimiento, actitudes, autoeficacia, el gusto, intención, hábito, percepción de barreras y preferencias), ambientales sociales (*modelamiento, apoyo parental activo, reglas exigidas y reglas permitidas por la familia*) y ambientales físicos (*accesibilidad en la casa, accesibilidad en la escuela y en el tiempo libre*)²⁴.

En las últimas tres décadas en México se han agravado los problemas de obesidad y sobrepeso, elevándose el interés por los beneficios preventivos del CF y V y por la utilización de instrumentos válidos y fiables en el campo epidemiológico y de la investigación empírica en niños de educación primaria. Por lo que, es importante contar con instrumentos que permitan explorar las relaciones entre factores psicosociales y el incremento de los niveles de CF y V; con el fin de diseñar estrategias de intervención efectivas en poblaciones escolares, a partir de las diferencias en los niveles de consumo^{10,13}. En el presente estudio se utilizó la versión mexicana del cuestionario PCHP, adaptada para niños escolares e informada en un estudio previo de validez de contenido y de constructo²⁵.

El objetivo del presente estudio es determinar la fiabilidad test-retest, la consistencia interna y la validez predictiva de los constructos de la versión mexicana del cuestionario PCHP, que evalúa factores psicosociales personales y ambientales asociados al CF y V en niños escolares de 10-12 años.

Material y métodos

Diseño

Se realizó un estudio transversal con un diseño test-retest, en el que se estableció un intervalo de 12 a 14 días entre las aplicaciones del mismo cuestionario.

Participantes

Una muestra total de 957 niños de 10 a 12 años participó en el estudio de fiabilidad y validez. La muestra fue obtenida de ocho escuelas primarias (17 grupos escolares de quinto y sexto grado) en Ciudad Juárez, Chihuahua, México durante los meses de octubre a diciembre de 2012. Las escuelas fueron seleccionadas tratando de representar los diferentes niveles socioeconómicos determinados por el contexto geográfico y socioeconómico de la ubicación de las escuelas. De los 1039 participantes el 92% (957) de los niños escolares respondieron el mismo cuestionario en las dos ocasiones que se administraron.

Instrumento

El instrumento utilizado para el presente estudio fue la versión mexicana del cuestionario PCHP, que mide

Tabla I
Fiabilidad de las escalas e ítems asociados al consumo de fruta en niños escolares

Constructos e ítems	Fiabilidad, Test-retest		Consistencia interna		
	# de ítems	CCI ^a , IC ^b 95%	Test Alfa	Retest Alfa	Alfa Inicial ^c
<i>Personales</i>					
Habilidades cognitivas	7	0,64 (0,60-0,69)	0,78	0,81	0,73
¿Cuánta fruta consideras que comes?					
¿Comparándote con la mayoría de los niños/as de tu edad, tu consumo de fruta es más o es menos?					
Me gusta comer fruta todos los días					
La mayoría de la fruta sabe bien					
Me resulta fácil comer fruta todos los días					
Quiero comer fruta todos los días					
Comer fruta todos los días es una costumbre, un hábito para mí					
Preferencias	11	0,66 (0,62-0,70)	0,76	0,78	0,75
Marca tu respuesta según sea tu gusto por cada fruta					
Listado de once frutas: plátanos, peras, naranjas, mandarinas, ciruelas, duraznos, melón, fresas, papaya, mango, piña					
Actitudes	4	0,66 (0,62- 0,70)	0,76	0,79	0,65
Comer fruta todos los días me hace sentirme bien					
Comer fruta todos los días me hace tener más energía					
Mis amigos/as comen fruta todos los días					
Si decido comer fruta todos los días, puedo hacerlo					
Percepción de barreras	4	0,66 (0,62-0,70)	0,75	0,78	0,63
No como fruta porque tardo mucho tiempo en comerla					
No como fruta porque se me antoja comer otra cosa, por ejemplo dulces o papitas					
No como fruta porque se me ensucian las manos al comerla					
No como fruta porque es difícil de llevar a la escuela					
<i>Percepción ambiental social</i>					
Modelamiento	5	0,61 (0,56-0,66)	0,76	0,74	0,72
Mi mamá come fruta todos los días					
Mi papá come fruta todos los días					
Mi mamá me anima a comer fruta todos los días					
Mi papá me anima a comer fruta todos los días					
¿Tus papás te piden que comas fruta todos los días?					
<i>Percepción ambiental física</i>					
Accesibilidad en la casa	8	0,60 (0,55-0,65)	0,67	0,72	0,76
¿En tu casa te permiten comer toda la fruta que quieras?					
¿En tu casa te permiten tomar todo el jugo de fruta que quieras?					
¿Si dices en tu casa que fruta te gustaría comer, la comprarían?					
¿Si dices en casa que jugo de fruta natural te gustaría tomar lo prepararían?					
¿Hay diferentes tipos de fruta en casa?					
La fruta que te gusta ¿la tienen en casa?					
¿El jugo de fruta que te gusta lo tienen en casa?					
¿En tu casa te prepara tu papá o tu mamá pedazos de fruta para comer cuando te dé hambre?					
Accesibilidad en la escuela	3	0,67 (0,63- 0,71)	0,54	0,60	0,55
¿Puedes conseguir fruta en la escuela, ya sea que la compres o te la regalen?					
¿Te ofrecen fruta cuando pasas la tarde en casa de tus amigos?					
¿Puedes conseguir fruta donde pasas tu tiempo libre como en el parque, clubes, centros deportivos, ya sea que la compres o te la regalen?					
<i>Frecuencia de consumo</i>					
¿Con qué frecuencia sueles comer fruta?	1	0,61 (0,55-0,65)	0,74	0,74	0,81

^aCoefficiente de correlación intraclase.

^bIntervalo de confianza.

^cAlfa inicial: consistencia interna en el estudio de validez de constructo²⁶.

siete constructos (*preferencias, habilidades cognitivas, actitudes, percepción de barreras, modelación, accesibilidad en la casa y accesibilidad en la escuela*) con 42

ítems asociados al consumo de fruta en una escala de cinco puntos (tabla I) y seis constructos (*preferencias, habilidades cognitivas, percepción de barreras, mode-*

Tabla II
Fiabilidad de las escalas e ítems asociados al consumo de verdura en niños escolares

Constructos/ítems	Fiabilidad, Test-retest		Consistencia interna, Alfa de Cronbach		
	# de ítems	CCI ^a , IC ^b 95%	Test Alfa	Retest Alfa	Alfa Inicial ^c
<i>Personales</i>					
Habilidades cognitivas	10	0,64 (0,59-0,68)	0,90	0,92	0,74
¿Cuánta verdura consideras que comes?					
¿Comparándote con la mayoría de los niños/as de tu edad, tu consumo de verdura es más o es menos?					
Comer verdura todos los días me hace sentirme bien					
Comer verdura todos los días me hace tener más energía					
Me gusta comer verdura todos los días					
La mayoría de la verdura sabe bien					
Me resulta fácil comer verdura todos los días					
Si decido comer verdura todos los días, puedo hacerlo					
Quiero comer verdura todos los días					
Comer verdura todos los días es una costumbre, un hábito para mí					
Preferencias	11	0,62 (0,57-0,66)	0,81	0,83	0,83
Marca tu respuesta según sea tu gusto por cada fruta					
Listado de doce verduras: tomate, col, espinacas, apio, ejotes, cebolla, zanahorias, brócoli, chícharos verdes, betabel, calabacitas					
Percepción de barreras	3	0,66 (0,61-0,70)	0,72	0,76	0,75
No como verdura porque tardo mucho tiempo en comerla					
No como verdura porque se me antoja comer otra cosa, por ejemplo dulces o papitas					
No como verdura porque es difícil de llevar a la escuela					
<i>Percepción ambiental social</i>					
Modelamiento	4	0,60 (0,55-0,65)	0,80	0,84	0,83
Mi mamá come verdura todos los días					
Mi papá come verdura todos los días					
Mi mamá me anima a comer verdura todos los días					
Mi papá me anima a comer verdura todos los días					
<i>Percepción ambiental física</i>					
Accesibilidad en la casa	5	0,60 (0,55-0,66)	0,80	0,80	0,75
¿Tus papás te piden que comas verdura todos los días?					
¿En tu casa te permiten comer toda la verdura que quieras?					
¿Si dices en casa que verdura te gustaría comer, la comprarían?					
¿Hay diferentes tipos de verduras en casa?					
¿La verdura que te gusta la tienen en casa?					
Accesibilidad en la escuela	3	0,68 (0,64-0,72)	0,76	0,77	0,70
¿Llevas verdura a la escuela?					
¿Puedes conseguir verdura en la escuela, ya sea que la compres o te la regalen?					
Puedes conseguir verdura donde pasas tu tiempo libre como en el parque, clubes, centros deportivos, ya que la compres o te la regalen?					
<i>Frecuencia de consumo</i>					
¿Con qué frecuencia sueles comer verdura?	1	0,66 (0,61-0,70)	0,75	0,73	0,81

^aCoefficiente de correlación intraclass.

^bIntervalo de confianza al 95%.

^cAlfa inicial: consistencia interna en el estudio de validez de constructo²⁶.

lación, accesibilidad en la casa y accesibilidad en la escuela) con 38 ítems en una escala de cinco puntos relacionados al consumo de verdura (tabla II)²⁶.

La estructura factorial del cuestionario PCHP incluyó los siguientes constructos: El primero, las preferencias a la fruta y la verdura, referida a lo que les

gusta o no a los niños; el segundo, las habilidades cognitivas asociados a la elección e incremento de conductas de CF y V, sustentadas en un marco conceptual presentado por Roschild²⁷, este constructo pertenece a la categoría de factores personales en el “Cuestionario PCHP”²⁶. Así los individuos con altas habilidades cog-

nitivas poseen mejores recursos mentales asociados a conductas saludables, es decir, habilidades de conocimiento o de aprendizaje, de razonamiento o de solución de problemas, autoeficacia y autocontrol para el CF y V²⁸. El tercer constructo fue referido a las actitudes o expectativas con respecto a resultados positivos de una conducta saludable o del CF y V; el cuarto, la percepción de barreras o percepción y resolución de obstáculos relacionados al CF y V; el quinto, el modelamiento de conductas mediante la observación de la conducta de otras personas del medioambiente social; sexto, la accesibilidad en la casa o la facilidad con la que los niños pueden encontrar fruta y verdura para su consumo en casa y séptimo, la accesibilidad en la escuela o la facilidad con la cual los individuos pueden encontrar frutas y verduras disponibles para su consumo en la escuela. Finalmente, se empleó un ítem para evaluar el consumo actual de fruta y verdura con el cual se estimó la frecuencia de CF y V: ¿Con qué frecuencia sueles comer fruta o verdura? [1] Nunca, [2] Menos de 1 día a la semana, [3] Un día a la semana, [4] 2 - 4 días a la semana, [5] 5-6 días a la semana, [6] Todos los días, una vez al día, [7] Todos los días, dos veces al día y [8] Todos los días, más de dos veces al día. En los cuadros 1 y 2 se muestran los constructos, ítems y escalas del cuestionario PCHP.

Procedimiento

El cuestionario fue administrado en dos ocasiones en el salón de clases a los mismos niños, con un intervalo de 12 a 14 días entre cada aplicación. La muestra fue recogida de manera incidental, tratando de obtener un porcentaje equivalente de niños y niñas, del nivel educativo y rango de edad. El requisito de participación fue estar cursando quinto y/o sexto grado de educación primaria. Se informó a los participantes que sus respuestas serían totalmente anónimas y confidenciales. Se utilizó el consentimiento pasivo de los padres respecto a la participación de sus hijos, el consentimiento de los niños al iniciar la aplicación del instrumento y la aprobación de las autoridades escolares. El estudio fue aprobado por el comité de bioética de la Universidad Autónoma de Ciudad Juárez.

Análisis estadísticos

El coeficiente alfa de Cronbach fue calculado para estimar la consistencia interna de las escalas y los valores a partir de 0,70 se consideraron como aceptables²⁹. A través de los coeficientes de correlación intraclass (CCI) se evaluó la confiabilidad test-retest con un intervalo de confianza del 95%, el rango de valores de los CCI de 0,51 a 0,70 fueron considerados como moderados, de 0,71 a 0,90 reflejaron una buena confiabilidad test-retest y de > 0,90 una excelente confiabilidad test-retest³⁰. Se empleó la prueba T² de Hotelling

con corrección Bonferroni para estimar la igualdad de medias entre el test y el retest para 13 escalas. Con la correlación de Spearman evaluó la validez predictiva de los constructos, las correlaciones fueron calculadas entre todos los predictores de fruta y verdura con la variable CF y V. Los datos fueron analizados mediante el Statistical Package for the Social Science (SPSS) v17.

Resultados

Características de la muestra

Una muestra de 957 niños escolares, compuesta por 486 (50,80%) niñas y 471 (49,20%) niños. El rango de edad varió de 10 a 13 años ($M = 11,8$; $DE = 0,74$), siendo la media para la niñas igual a 11,06 ($DE = 0,67$) y para los niños 11,06 ($DE = 0,70$). Por nivel escolar, 486 participantes (50,80%) cursaban el Quinto Grado (25,71% de niñas y 25,09% de niños) y 471 (49,20%) Sexto Grado (25,08% de niñas y 24,12% de niños) de educación primaria.

Fiabilidad test-retest

Las tablas I y II muestran los valores de las CCI de los constructos de fruta y verdura. La confiabilidad test-retest fue moderada ($CCI > 0,60$) en siete de siete constructos del consumo de fruta y en seis de seis constructos del consumo de verdura con un intervalo de confianza del 95%. El rango de valores de los CCI para las escalas de fruta y verdura fue entre 0,60 y 0,68. En general la percepción de las escalas fue mejor en las de fruta que en las de verdura. No se encontraron diferencias significativas en los puntajes de las medias de la T² de Hotelling para las 13 variables psicosociales, a excepción de las preferencias, $F = (13,1912) = 62,15$ $p = 0,01$ y la accesibilidad en la casa, $F = (13,1912) = 47,28$, $p = 0,01$.

Consistencia interna de las escalas

La consistencia interna fue de baja a alta, los valores alfa de Chronbach calculados para el test y el retest resultaron ser un poco más altos en las escalas de verdura (rango de 0,72 a 0,92) que en las de fruta (rango: 0,54 a 0,81). Se encontraron valores alfa mayores a 0,70 en cuatro de seis escalas de fruta (*habilidades, preferencias, percepción de barreras, modelación y accesibilidad en la casa*) y en seis de seis escalas de verdura (*habilidades, preferencias, percepción de barreras, modelación, accesibilidad en la casa y accesibilidad en la escuela*). Una escala de fruta (*accesibilidad en la escuela*) obtuvo valor inferior a 0,70 (test, $\alpha = 0,54$; retest, $\alpha = 0,60$). Cuatro escalas de verdura obtuvieron un rango de valores alfa entre 0,80 y 0,92 (*habilidades*

Tabla III
Validez predictiva de las escalas para evaluar factores asociados al consumo de fruta y verdura en niños escolares (correlación de Spearman)

Constructos	Consumo de fruta Correlación ^a	Consumo de verdura Correlación ^a
<i>Personales</i>		
Habilidades cognitivas	0,51**	0,60**
Preferencias	0,38**	0,49**
Actitudes	0,23**	N/A
Percepción de barreras	-0,36**	-0,40**
<i>Percepción social ambiental</i>		
Modelamiento	0,24**	0,35**
<i>Percepción física ambiental</i>		
Accesibilidad en la casa	0,27**	0,48**
Accesibilidad en escuela	0,14**	0,30**

N/A: el dato no es aplicable.

^aSignificancia estadística.

**P < 0,01.

cognitivas, preferencias, percepción de barreras, modelación y accesibilidad en la casa) y dos escalas resultaron con valores alfa en un rango de 0,70 a 0,80 (accesibilidad en la escuela y frecuencia de consumo).

Validez predictiva

La validez predictiva de los datos del cuestionario incluyeron el calculo respectivo de las correlaciones de Spearman entre las escalas de los factores determinantes del CF y V y la frecuencia de CF y V (tabla III). Todas las correlaciones resultantes fueron significativas para el total de la muestra. La validez predictiva de los factores determinantes personales del CF y V fue de moderada a buena, en un rango entre 0,23 y 0,51 en fruta y de 0,40 a 0,60 en verdura. Las correlaciones entre los factores determinantes ambientales (sociales y físicos) fueron bajas, en un rango de 0,14 a 0,27 en fruta, exceptuando las escalas de verdura cuyo rango fue de 0,30 a 0,48.

Discusión

El objetivo del presente estudio fue determinar las propiedades psicométricas de la versión mexicana del cuestionario PCHP, a partir de la propuesta original del cuestionario²⁴ y ante la ausencia de estudios que avalen dichas propiedades en población escolar mexicana. Los resultados mostraron una moderada fiabilidad test-retest en todos los constructos y una consistencia interna de moderada a alta en la mayoría de las escalas, excepto en la escala de accesibilidad a la fruta en la escuela. La validez predictiva de los factores psicosociales personales y ambientales fue de moderada a buena. Por lo que, este instrumento puede ser aplicable

para la evaluación global de factores personales y ambientales del CF y V en niños escolares de 10 a 12 años.

En general, confiabilidad test-retest fue satisfactoria, las correlaciones obtenidas fueron mayores a 0,60 en un rango de 0,60 a 0,68, comparable al estudio de De Bourdeaudhuij et al, con el mismo cuestionario, cuyas correlaciones intraclase fueron de moderadas a buenas, mayores a 0,60 en 12 de 15 constructos relacionados con la fruta y en 12 de 15 constructos asociados con la verdura dentro de un rango de 0,50 a 0,80²⁴. Asimismo, Bere y Klepp en un estudio con un cuestionario conformado con siete factores psicosociales, cuatro de ellos personales (intención, preferencia, autoeficacia y conocimiento) y tres ambientales (modelamiento, accesibilidad en la casa y accesibilidad en la escuela) asociados al CF y V obtuvieron un rango de correlaciones test-retest de 0,51 a 0,75¹⁸. Además, Norman et al, reportaron una confiabilidad test-retest de moderada a buena (0,63-0,79) en un estudio con una escala breve de medición de factores psicosociales del CF y V en niños de 10 a 12 años³¹. Igualmente, Wilson, Magarey y Materson informaron correlaciones intraclase de variables personales y ambientales del CF y V en un rango entre 0,16 y 0,66. Así también Bannink y van der Bijl reportaron índices de correlación intraclase que variaron entre 0,33 y 0,84 al aplicar dos instrumento empleados para la evaluación de la autoeficacia en el consumo de fruta y verdura³³. Sin embargo, también se han reportado problemas de baja confiabilidad test-retest al emplear factores psicosociales en una escala de accesibilidad a jugo, fruta y verdura (CCI = 0,23) y otra de disponibilidad a fruta, jugo y verdura (CCI = 0,23)³⁴. Por lo que, se puede concluir que en la línea de lo informado en los estudios anteriormente mencionados, nuestros datos encontrados de fiabilidad test-retest en factores psicosociales asociados con el CF y V, se ubican dentro de los rangos reportados que tiende a ser de moderados a buenos.

Se analizó la consistencia interna de las escalas, en general los coeficientes Alfa de Chronbach en este estudio fueron de bajos a altos (rango: 0,54 a 0,92), comparables a los reportados en el estudio original (rango: 0,52 a 0,89)²⁴. En el presente estudio se esperaba que el cuestionario al contener un menor número de factores con mayor número de ítems en comparación con la estructura factorial del estudio original, ésta fuese mejor sobre todo en los factores conformados con un mayor número de ítems, sin embargo, la consistencia interna no fue muy alta y resultó semejante a la mostrada en algunos estudios previos que emplearon una selección reducida de factores psicosociales asociados al CF y V en niños y adolescentes³¹⁻³³. Tal vez, la consistencia interna en nuestro estudio puede ser atribuible a las características de la medición empleada en el autoinforme o a las tendencias de respuesta de los participantes o a la variabilidad en la estabilidad de los datos.

Finalmente, la validez predictiva de las escalas fue de moderada a buena. Al comparar la validez predic-

tiva de nuestro trabajo con el estudio original se observaron resultados similares. En general las correlaciones del estudio original fueron de moderadas a buenas y los factores personales mostraron un rango de -0,20 a 0,54 en fruta y de -0,16 a 0,54 en verdura. Sin embargo, en los factores ambientales (sociales y físicos) el rango de correlaciones fue de bajo a moderado (de 0,05 a 0,38)²⁴. En otros estudios de validez predictiva mediante correlaciones de Spearman, los rangos oscilaron de 0,27 a 0,46 comparable a los resultados del presente estudio^{32,33}. Los datos de las correlaciones encontradas en el presente estudio son las primeras evidencias de la estimación de las correlaciones entre las escalas asociadas al CF y V. Por lo que, será conveniente que en futuros estudios se analicen las relaciones entre los constructos mediante herramientas de análisis multivariante con muestras representativas de otros contextos regionales mexicanos para incrementar la validez predictiva de este cuestionario.

Una de las contribuciones de este estudio fue someter a evaluación de fiabilidad y validez predictiva, la estructura factorial hallada en la adaptación de este cuestionario en población escolar mexicana²⁶, que resultó diferente a la propuesta por De Bourdeaudhuij et al. Nuestros datos favorecen la conformación de factores, como el factor de habilidades cognitivas, que puede actuar como mediador o predictor del CF y V. Además este constructor podría relacionarse con conducta nutricional, actividad física y peso corporal²⁸. Estas relaciones podrían explorarse en futuras investigaciones con modelos causales a través del uso de ecuaciones estructurales para explicar el CF y V con base a éste y otros factores determinantes personales y ambientales. Asimismo se podrían considerar las diferencias en el consumo en función del género o nivel socioeconómico en muestras representativas, en lugar de las muestras utilizadas en nuestro estudio.

Una de las limitantes del presente estudio fue la utilización de una muestra por conveniencia, que no permite que los hallazgos se puedan generalizar a toda la población de niños escolares. Por lo que, es necesario que en futuros estudios se trabaje con muestras representativas procedentes de otros contextos regionales mexicanos. Además de la realización de estudios que se dirijan al incremento de evidencias de validez y fiabilidad del cuestionario PCHP para reforzar la pertinencia de su uso en contextos escolares.

Conclusión

En conclusión los resultados de este estudio demuestran una fiabilidad y validez suficiente de la versión mexicana del “Cuestionario PCHP” para la evaluación global de factores psicosociales personales y ambientales del consumo de fruta y verdura en niños escolares de 10 a 12 años.

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Original / *Obesidad*

Self-perceived weight status, dieting and unhealthy weight-control behaviors among Spanish male adolescents

Carlos A. Almenara^{1,2}, Jordi Fauquet^{3,4}, Gemma López-Guimerà², Montserrat Pamiás Massana⁵ and David Sánchez-Carracedo²

¹Institute for Research on Children, Youth and Family. Department of Psychology. Faculty of Social Studies. Masaryk University. Brno. Czech Republic. ²Unit for Research on Eating and Weight-related Behaviors. Dept. Clinical and Health Psychology. Universitat Autònoma de Barcelona. Barcelona. Spain. ³Dept. Psychobiology and Methodology of Health Sciences. Universitat Autònoma de Barcelona. Barcelona. Spain. ⁴Neuroimaging Research Group. IMIM (Hospital del Mar Medical Research Institute). Barcelona Biomedical Research Park. Barcelona. Spain. ⁵Mental Health Unit of the Parc Taulí Health Corporation (CSPT). Sabadell. Barcelona. Spain.

Abstract

Introduction: Self-perceived weight status among adolescents has been associated with weight-control behaviors. However, this relationship varies across weight status.

Objectives: The aim of this study was to examine the effect of self-perceived weight status on dieting and unhealthy weight-control behaviors among Spanish male adolescents, across weight status.

Method: Participants were 597 Spanish male adolescents ($M = 13.94$ years old, $SD = 0.60$). Body weight and height were measured in situ. Self-perceived weight status, dieting, and unhealthy weight-control behaviors were evaluated.

Results: The adolescents were inaccurate on estimating their weight status. Those who were overweight or obese, or who perceived themselves to be so, were more likely to report dieting and unhealthy weight-control behaviors.

Discussion: There is a need to promote healthier eating behaviors among adolescents, and to take into account the fact that self-perceived weight status may hinder the adoption of such behaviors.

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Key words: *Body image. Body weight. Adolescent. Sex factors. Weight loss. Self-perceived weight status.*

ESTATUS DE PESO PERCIBIDO, DIETA Y CONDUCTAS NO SALUDABLES DE CONTROL DEL PESO EN ADOLESCENTES VARONES ESPAÑOLES

Resumen

Introducción: El estatus de peso percibido se ha asociado a conductas de control del peso en adolescentes. Esta relación varía de acuerdo al estatus de peso corporal.

Objetivos: Explorar el efecto del estatus de peso percibido sobre la práctica de dieta y conductas no saludables de control del peso en adolescentes varones españoles, considerando su estatus de peso.

Método: Participaron 597 adolescentes ($M = 13,94$ años, $DS = 0,60$). Se registró in situ la talla y peso corporal. Se evaluó el peso percibido, la práctica de dieta y conductas no saludables de control del peso.

Resultados: Los adolescentes fueron inexactos al estimar su estatus de peso. Aquellos con sobrepeso, obesidad o los que se percibían como tales, fueron los que más informaron hacer dieta y conductas no saludables de control del peso.

Discusión: Es necesario promover conductas alimentarias saludables entre los adolescentes y considerar que el estatus de peso percibido puede limitar la adopción de estos comportamientos.

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Palabras clave: *Imagen corporal. Peso corporal. Adolescente. Factores de sexo. Pérdida de peso. Peso percibido.*

Correspondence: Carlos A. Almenara.
Institute for Research on Children, Youth and Family.
Faculty of Social Studies. Masaryk University.
Joštova, 10.
602 00 Brno. Czech Republic.
E-mail: carlos.almenara@mail.muni.cz

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Abbreviations

UWCB: Unhealthy weight-control behaviors.

SD: Standard deviation.

MABIC: Medios de comunicación, alimentación alterada, burlas relacionadas con el peso e insatisfacción corporal.

CSPT: Corporació Sanitària Parc Taulí.

BMI: Body Mass Index.

EAT: Eating Among Teens.

Introduction

Dieting and unhealthy weight-control behaviors (UWCB), such as fasting, eating very little and skipping meals are common behaviors among adolescents trying to lose weight.¹ Unfortunately, these behaviors tend to take place in a naturalistic way (ie without professional advice), increasing the risk of unhealthy eating patterns and weight gain over time.¹ Several external factors may contribute to promoting these UWCB among adolescents. For instance, the multi-billion dollar weight-loss industry, public health campaigns for tackling the so-called “obesity epidemic” or pressure from peers and parents may, directly or indirectly, encourage adolescents to adopt UWCB so as to lose weight. Even so, other, more individual factors can also facilitate the adoption of UWCB.

A significant individual factor is self-perceived body weight (ie how we perceive our own body weight). However, few studies have taken into account that this self-perception may vary by weight status, and may influence the adoption of eating and weight-related behaviors in different ways. In particular, an inaccurate self-perception of body weight can promote the adoption of unhealthy eating patterns and behaviors among the overweight and obese,² and increase the risk of weight preoccupations and weight control among normal-weight adolescents.³

In addition, recent studies have revealed secular trends over time in relation to self-perceived body weight among Spanish adolescents.⁴ Specifically, such research found a pattern of change toward the underestimation of overweight status, suggesting that the steady increase of the overweight population may make weight misperception more likely, especially among overweight men. Thus, it is important in this context to examine the role of self-perceived body weight in relation to the adoption of dieting and UWCB.

Accordingly, the aim of the present study was to examine the role of self-perceived weight status in dieting and UWCB among Spanish male adolescents of different weight status.

Method

Sample and procedure

The sample comprised 597 boys (13 to 16 years old; $M = 13.94$, $SD = 0.60$), predominantly middle-class

(79.5%).⁶ Self-reported origin was typically Spanish (73.8%), followed by Latin-American (12.2%), mixed parentage (5.4%), North African (3.2%), European (2.5%), Sub-Saharan (1.2%), and other (1.7%). Participants were part of the MABIC project, a longitudinal research project on the prevention of eating- and weight-related problems among adolescents of both sexes from Barcelona (Spain).⁵ The study followed the ethical guidelines of the Helsinki Declaration (as revised in Edinburgh, 2000). The protocol was approved by the Clinical Research Ethics Committee of the “Parc Taulí” Health Corporation (CSPT). A detailed description of the methodology has been reported previously.⁵

Materials

Measured weight status. Height and weight were measured *in situ*. Body mass index ($BMI = kg/m^2$), was calculated and used to obtain weight-status categories (underweight, normal weight, overweight, obese), using international cut-off points for age and sex.^{7,8}

Self-perceived weight status. Participants were asked “What do you think is your current weight level?” Response options were: underweight, normal weight, slightly overweight, very overweight.

Dieting. Based on Project EAT,⁹ participants were asked “How often have you gone on a diet during the last year?” Next to the question the term diet was defined as “changing the way you eat so you can lose weight”. Response options were: “never”, “one to four times”, “five to 10 times”, “more than 10 times”, and “I am always dieting”. Following previously-reported criteria,¹⁰ respondents who reported having dieted at least once were classified as dieters.

Unhealthy weight-control behaviors (UWCB). Also based on Project EAT, participants were asked “Have you done any of the following things in order to lose weight or keep from gaining weight in the past year?” Response options were: “skipped meals”, “fasted”, “ate very little food”, “smoked more cigarettes”, “used a food substitute”, “made myself vomit”, “took diet pills”, “used laxatives”, and “used diuretics”. Response format was dichotomous (‘yes’, one point; ‘no’, zero points). As in previous studies,¹⁰ respondents reporting at least one behavior were classified as engaging in UWCB.

Data Analyses

First, descriptive analyses were performed to examine the sample in terms of weight status (measured, self-perceived), and behaviors (dieting, UWCB). Second, logistic regression analysis was used to obtain the odds of dieting and then of UWCB. Each logistic regression was controlled for age, ethnicity, and socioeconomic status. Predictors were measured weight status and self-perceived weight status.

Table I
Self-perceived weight status by measured weight status*

	Measured weight status				Total
	UW [†]	NW [‡]	OW [§]	OB	
N	49	384	116	44	
<i>Self-perceived weight status</i>					
Underweight	55.1	9.9	0	0	10.9
Normal weight	42.9	85.1	40.5	9.1	66.9
Slightly overweight	0	5.0	58.6	77.3	20.6
Very overweight	2.0	0	0.9	13.6	1.5
Total	8.3	64.8	19.6	7.4	100

*Data is given as percentage. Total n values may differ because of incidental missingness.

[†]UW = underweight.

[‡]NW = normal weight.

[§]OW = overweight.

^{||}OB = obese.

Results

Mean BMI was 20.94 ($SD = 4.18$); 44 boys were obese (7.4%), 116 overweight (19.6%), 384 normal weight (64.8%) and 49 underweight (8.3%).

Self-perceived weight status

Comparing measured weight status with self-perceived weight status (table I), only 13.6% of obese adolescents self-perceived as very overweight, 40.5% of overweight adolescents self-perceived as normal weight, and 42.9% of underweight adolescents self-perceived as normal weight. These results indicate that a substantial number of adolescents were inaccurate on estimating their weight status.

Dieting and unhealthy weight-control behaviors

In descriptive terms, a total of 25.6% of adolescents were classified as dieters (8.2% of underweight, 12.5% of normal weight, 55.2% of overweight, and 77.3% of obese). Regarding UWCB, 25% of adolescents reported at least one UWCB (20.4% of underweight, 17.4% of normal weight, 38.8% of overweight, and 56.8% of obese). These results indicate that a high percentage of overweight and obese adolescents reported being engaged in dieting and UWCB. Notably, some already underweight boys also reported dieting and UWCB.

Dieting and unhealthy weight-control behaviors by measured weight status and by self-perceived weight status

The underweight group ($n = 49$), was removed from subsequent analyses because of the small number of cases reporting dieting and UWCB in each category.

Next, and before carrying out the logistic regression analyses, measured weight status and self-perceived weight status were reduced to two categories each. Thus, measured weight-status categories were reduced to (1) normal weight and (2) overweight, including obese; self-perceived weight-status categories were reduced to (1) self-perceived normal weight and (2) self-perceived slightly overweight or very overweight.

Table II shows the odds of dieting and UWCB from the logistic regression analyses.

The odds of dieting and UWCB were statistically significant on comparing those who were either overweight or obese (or self-perceived as such), with those who were normal weight (or self-perceived as such). These results indicate that, in general, either being or self-perceiving as overweight or obese increases the

Table II
Odds Ratio (OR) indicating the effect of weight status on dieting and unhealthy weight-control behaviors (UWCB)*

Variables	OR	Wald	95% CI
<i>Dieting</i>			
MWS [†]	10.74	108.95	6.88-16.77
SPWS [‡]	11.15	103.61	7.01-17.73
MWS × SPWS [§]	12.71	105.55	7.83-20.65
<i>UWCB</i>			
MWS	3.47	34.38	2.29-5.27
SPWS	2.74	21.19	1.78-4.22
MWS × SPWS	2.79	20.31	1.79-4.37

*Analyses were adjusted by ethnicity, age, and socioeconomic status. Weight status categories (measured, self-perceived) were: normal weight and overweight including obese. Reference group was normal weight. Results in bold were significant ($p < 0.001$).

[†]MWS = measured weight status.

[‡]SPWS = self-perceived weight status.

[§]MWS × SPWS = interaction between these two variables.

risk of dieting and UWCB. It is noteworthy that the risk of dieting was slightly higher among those who self-perceived as overweight or obese. In contrast, the risk of UWCB was slightly higher among those who were actually overweight or obese.

Discussion

The aim of the present study was to examine the effect of self-perceived weight status on dieting and UWCB among Spanish male adolescents of different weight status.

We found that overweight and obese adolescents tended to underestimate their weight status, whereas underweight adolescents tended to overestimate it. This finding has been reported previously,³ and merits further attention. For example, weight-related norms (eg what is perceived as a normal body weight in a given context) may influence how adolescents perceive and estimate their body size.¹¹ These social norms are commonly linked to an ideal of beauty or attractiveness in a given context.¹² In Western countries such as Spain, boys may be aware of a male beauty/attractiveness ideal (eg a lean and muscular body), and may perceive sociocultural pressure (eg messages from peers and the media) to attain this ideal.¹³ Thus, overweight and obese adolescents might underestimate their weight because of the double burden of sociocultural pressure and the stigma of obesity.¹⁴ This could have a strong influence on how they perceive and estimate their body size,¹⁵ to the extent that they may reject referring to themselves as overweight or obese. Alternatively, it may be that these overweight and obese adolescents perceive their weight as “normal” given the steady increase in the proportion of overweight and obese adolescents in Spain.⁴ However, these ideas remain speculative, and further research is recommended. Furthermore, given the frequency of weight underestimation among overweight and obese adolescents, future studies should use caution on considering obesity prevalence based on self-reported data. In addition, the finding whereby underweight boys overestimate their weight could be explained by their having perceived their body size as closer to the ideal, so that they estimate their weight as “normal”. Notably, few studies have examined weight overestimation among underweight boys.³ Most probably, boys in this group have a body image disturbance, an eating disorder, or a higher risk of developing an eating disorder.³ Nevertheless, this cannot be supported by our findings. Therefore, future studies evaluating body image attitudes and behaviors among underweight boys who overestimate their weight are recommended. Finally, professionals in the public health field must bear in mind that weight misperceptions among adolescents, either underestimation or overestimation, can interfere with the implementation of strategies for promoting healthy eating- and weight-related behaviors.²

As regards the prevalence of dieting and UWCB by weight status, the highest prevalence was found among obese adolescents. However, it should be noted that some already underweight boys also reported these behaviors. This finding is consistent with those of previous studies,^{1,10,16} and highlights once more the importance of examining eating- and weight-related behaviors separately by weight status, as well as the need to further evaluate the risk of disordered eating among those in the extreme categories.

We also examined the effect of measured weight status and self-perceived weight status on the risk of dieting and UWCB. Our results suggest that either being or perceiving oneself as overweight or obese substantially increases the risk of dieting and UWCB, compared to being or self-perceiving normal weight. Notably, the risk of dieting was slightly higher if boys self-perceived as overweight or obese. This finding is consistent with the previous literature, including a large cross-national study.¹⁶ However, it is also noteworthy that the risk of UWCB in our sample was slightly higher if boys were actually overweight or obese. Thus, our results may again suggest that other factors, such as weight-related norms,¹¹ may influence the risk of dieting and UWCB. For instance, it may be commonly accepted among these boys to engage in dieting if they are or self-perceive as overweight or obese. However, this idea remains speculative, and future studies should assess the role of social norms in relation to dieting and UWCB on comparing measured and self-perceived weight-status categories. In any case, these adolescents may be engaging in dieting behaviors without professional advice, and this can increase their risk of unhealthy eating patterns.¹ Consequently, health professionals should be aware of these behaviors and how self-perceived weight might influence eating patterns and behaviors of adolescents. Finally, and with a view to avoiding unintended potentially harmful effects such as promoting weight stigmatization and weight concerns, health professionals should help adolescents to adopt healthy eating- and weight-related behaviors focusing more on their overall wellness than exclusively on weight loss.¹⁷

This study has some limitations, and its results should be interpreted with caution. First, this is a cross-sectional study, so that the inferences that can be made are limited; more longitudinal studies are necessary. Second, our sample is not representative of the entire population of Spanish male adolescents, and few participants were in the extreme weight-status categories (underweight, obese). For these reasons, any generalizations should be made with care. Finally, we used some self-report measures that could bias the results due to under-reporting or over-reporting of behaviors. However, our study has some important strengths and implications. Few studies have examined the effect of self-perceived weight status on dieting and UWCB by including an objective measure of body weight and height, and by controlling for recognized

confounding variables. Objective measures of weight and height generate more accurate data than self-reported measures. Additionally, we used international cut-off points to establish weight status, and these are recommended so as to allow comparability among surveys.¹⁸ Furthermore, logistic regression analyses were done by controlling for ethnicity and socioeconomic status, variables widely acknowledged to influence self-perceived weight.¹¹ Finally, our results on weight misperception are of great importance for future research. Weight misperception may be associated with weight-related norms referring to a normative perceptual threshold for overweight in specific populations,¹¹ or to the trends in body weight misperception observed over the last decades,⁴ and this is a clear hint for professionals in the obesity field to give greater attention to self-perceived weight status.

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Original / *Obesidad*

Diferencias en los hábitos de alimentación y ejercicio físico en una muestra de preadolescentes en función de su categoría ponderal

Mireia Orgilés, Isabel Sanz, José Antonio Piqueras y José Pedro Espada

Universidad Miguel Hernández de Elche. España.

Resumen

Fundamentos: La obesidad es un problema con graves repercusiones para la salud física, psicológica y social que afecta a millones de niños y adolescentes en todo el mundo. Los objetivos de este estudio son obtener datos actualizados de la prevalencia de la obesidad y el sobrepeso en preadolescentes de 10 a 12 años de la provincia de Alicante, obtener información sobre los hábitos alimentarios, la actividad física y determinadas variables sociodemográficas, y examinar su relación con la obesidad y el sobrepeso infantil o el riesgo de padecerlos.

Método: Participaron 623 preadolescentes, el 49,9% de sexo masculino y el 50,1% femenino. El IMC se determinó siguiendo los criterios de la WHO Child Growth Standards.

Resultados: Se ha encontrado una alta prevalencia de obesidad y sobrepeso en nuestra provincia, el 20,4% y 34% respectivamente. Los resultados no mostraron diferencias estadísticamente significativas entre las categorías ponderales en las variables sexo, edad y nivel de estudios de los progenitores. Respecto a los hábitos de alimentación y ejercicio físico, los resultados sugieren que los niños y niñas con normopeso hacen un mayor número de comidas al día y, los niños con normopeso comen con mayor frecuencia en comedores escolares. Y apuntan a que los niños con normopeso realizan con mayor frecuencia ejercicio físico que los que presentan sobrepeso y obesidad, y que las niñas obesas utilizan más horas de ocio sedentario que las que presentan sobrepeso.

Conclusión: Los resultados refuerzan la necesidad de desarrollar programas eficaces de prevención e intervención temprana para la obesidad infantil.

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Palabras clave: *Obesidad. Sobrepeso. Infantil. Adolescente. Hábitos alimentarios. Ejercicio físico.*

DIFFERENCES IN EATING HABITS AND PHYSICAL ACTIVITY IN A SAMPLE OF PREADOLESCENT DEPENDING ON THEIR WEIGHT CATEGORY

Abstract

Background: Obesity is a problem with serious implications for the physical, psychological and social health that affects millions of children and adolescents worldwide. This study wants to obtain updated prevalence data of obesity and overweight in adolescents from 10 to 12 years old in the province of Alicante, information on eating habits, physical activity and selected sociodemographic variables. It is important to examine their relation with children's obesity and overweight or at risk of suffering it.

Methods: A total of 623 preteens participated, 49.9% male and 50.1% female. The IBM was determined following the WHO Child Growth Standards.

Results: It was found a high prevalence of obesity and overweight in our province: 20.4% and 34% respectively. The results showed no statistically significant differences between the categories by sex, age and educational level of parents. Regarding eating habits and of physical exercise, the results suggest that children with normal weight make more meals per day, and boys with normal weight eat more often in school canteens. Also it is suggested that boys with normal weight perform exercise more often than those who are overweight and obese, and obese girls use more hours of sedentary leisure than overweight girls.

Conclusion: The results reinforce the need to develop effective prevention and early intervention programs for childhood obesity.

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Key words: *Obesity. Overweight. Child. Teen. Eating habits. Physical exercise.*

Correspondencia: Mireia Orgilés.
Universidad Miguel Hernández de Elche.
Departamento de Psicología de la Salud.
Avda. de la Universidad s/n.
03202 Elche. Alicante. España.
E-mail: morgiles@umh.es

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Introducción

La obesidad es una enfermedad crónica y compleja que se caracteriza por la acumulación excesiva de grasa corporal. Suele iniciarse en la infancia o en la adolescencia y surge de una interacción genética y ambiental^{1,2}. Repercute negativamente en la calidad de vida relacionada con la salud infanto-juvenil³ y, aunque a corto plazo la obesidad infantil no se asocia a unas tasas de mortalidad elevadas, supone un mayor riesgo de consecuencias adversas para la salud y mortalidad prematura en la vida adulta^{4,5,6}. La obesidad es además un potente predictor de la obesidad en la adolescencia⁷ y en la adultez⁸ sobre todo cuando cursa en la segunda década de la vida². Se trata de la alteración metabólica más frecuente entre los 3 y los 14 años de edad y parece que así lo seguirá siendo en el futuro⁹. Numerosos son los estudios que relacionan la obesidad con el riesgo de padecer diversas complicaciones y enfermedades como la diabetes tipo 2, hipertensión, dislipemias, hipercolesterolemia, problemas cardiovasculares, articulares y digestivos^{1,4,6}. También se asocia con alteraciones en la respuesta inmune con un aumento en la propensión a infecciones, con cambios endocrinos como disminución de la respuesta de la hormona del crecimiento o hiperleptinemia^{10,11} y algunos tipos de cáncer, como el de mama, endometrio, vesícula, colon, recto y próstata^{1,12}. Además, se relaciona con alteraciones menstruales, esterilidad así como problemas respiratorios nocturnos, apnea del sueño y asma^{1,3,13}. A todos estos trastornos físicos hay que sumarle los problemas psicológicos y sociales provocados por la obesidad. Entre los más frecuentes destaca la baja autoestima, auto-imagen negativa sobre todo durante la adolescencia, introversión, aislamiento y rechazo social^{14,15,16}. También están relacionados con la obesidad y el sobrepeso infantil y juvenil los comportamientos compulsivos e impulsivos^{14,17}, la ansiedad, depresión, alteraciones de la conducta alimentaria con pérdida de control^{16,18}, e incluso la enuresis¹⁹.

Es complejo precisar la prevalencia de la obesidad en niños y adultos debido a los diferentes criterios y métodos de valoración utilizados para su diagnóstico¹⁵. Se estima que la prevalencia mundial de obesidad infantil y juvenil ha aumentado en las últimas décadas de un 4,2% en 1990 a un 6,7% en 2010 y se espera que esa tendencia alcance el 9,1% en 2020²⁰. A nivel mundial se calcula que 170 millones de niños menores de 18 años tienen sobrepeso⁵. Las tasas de prevalencia más altas se encuentran en los países desarrollados y las más bajas en los que están en vías de desarrollo; sin embargo, el sobrepeso está aumentando en casi todos los países, siendo los países de ingresos medio-bajos los que presentan unas tasas de crecimiento más rápido²¹. En comparación con el resto de países de Europa, España se sitúa en una posición intermedia en el porcentaje de adultos obesos. Sin embargo, en lo que se refiere a población infantil, España presenta una de las cifras más altas, tan sólo superadas por Italia, Malta

y Grecia, siguiendo así con la tendencia de otros países con problemas históricos de obesidad y sobrepeso como Estados Unidos y el Reino Unido²². Los datos más amplios sobre la prevalencia del problema en España proceden principalmente de las Encuestas Nacionales de Salud y de dos estudios: el estudio enKid (1998-2000) realizado en una población de 2 a 24 años que sitúa la prevalencia de obesidad en el 13,9% y la de sobrepeso y obesidad en el 26,3% (sólo sobrepeso 12,4%)², y el estudio ALADINO (Alimentación, Actividad física, Desarrollo Infantil y Obesidad) desarrollado durante el curso escolar 2010-2011 por la AESAN (Agencia de Seguridad Alimentaria y Nutrición) con niños de 6 a 9 años que refiere un 18,3% de niños obesos y un 26,2% con sobrepeso tomando como referencia los estándares de crecimiento de la OMS. En este último estudio se compararon los resultados obtenidos con los del enKid, y se observó que el crecimiento del sobrepeso parecía haberse estabilizado, puesto que no se encontraron diferencias significativas entre ambos estudios. En cuanto a la obesidad, sólo se halló un aumento en las niñas, mientras que en los niños la tendencia también parecía ser estable²³. Según los resultados preliminares de la última Encuesta Nacional de Salud de 2011-2012²⁴, la prevalencia de obesidad y sobrepeso en niños y adolescentes de 2 a 17 años se sitúa en el 27,8%. Estos resultados, junto a estudios recientes, indican una tendencia de estabilización en los últimos años de la prevalencia en España y en otros países desarrollados^{23,25}. El estudio enKid refiere las tasas más elevadas en Canarias y las zonas del sur y el levante español². En el caso de la Comunidad Valenciana la prevalencia es muy elevada, con un 22,28% de niños de 9 a 12 años que presenta obesidad o sobrepeso²⁶. En la provincia de Alicante la prevalencia de la obesidad entre los 6 y 11 años oscila entre el 13,5% y el 18,8%²⁷.

En general las tasas de prevalencia más altas tanto para la obesidad como para el sobrepeso las presentan los niños varones^{2,23} y en edades prepuberales^{2,28}. Sin embargo, en la provincia de Alicante no se han encontrado diferencias estadísticamente significativas respecto al sexo y la edad²⁷. Varios estudios señalan que la obesidad es más prevalente en familias y ambientes más desfavorecidos, con un menor nivel socioeconómico y educacional^{2,3,29,30}, en niños que comen poca fruta, verdura o legumbres y comen más bollería, pastelería y aperitivos^{27,31,31}, que no desayunan o toman un desayuno de baja calidad^{2,29} y que hacen pocas comidas al día³². También se ha encontrado un mayor número de niños con normopeso que comen habitualmente en comedores escolares^{29,31}. Respecto a los hábitos de ejercicio físico se ha observado mayor prevalencia de obesidad y sobrepeso en niños que realizan poca actividad física y hacen uso de más ocio sedentario^{29,33}.

Los objetivos del presente estudio son obtener datos actualizados de la prevalencia de la obesidad y el sobrepeso en preadolescentes de 10 a 12 años, obtener información sobre los hábitos alimentarios, la activi-

dad física y determinadas variables sociodemográficas, así como examinar su relación con la obesidad y el sobrepeso infantil o el riesgo de padecerlos. Se espera encontrar diferencias significativas entre los preadolescentes con obesidad y/o sobrepeso y aquéllos con normopeso en las variables analizadas (sexo, edad, nivel educativo de los padres, hábitos de alimentación y actividad física). Conocer la dimensión epidemiológica del problema y las variables relacionadas permitirá iniciar tareas de prevención y tratamiento más efectivas y adaptadas a las necesidades de esta población.

Método

Participantes

Se trata de un estudio transversal en el que participaron 623 preadolescentes de edades comprendidas entre los 10 y 12 años ($M = 11,03$; $DT = 0,7$), el 49,9% de sexo masculino ($M = 11,06$; $DT = 0,7$) y el 50,1% femenino ($M = 11,01$; $DT = 0,7$). El 85,9% de los participantes eran españoles y el resto eran nacidos en otros países. Respecto a su situación familiar, el 82,1% tenían padres casados, el 16,4% padres separados o divorciados, el 0,2% tenían padre o madre solteros, y el 1,4% eran huérfanos de un padre o de los dos. La mayoría de los participantes tenían un solo hermano (62%), el 16,4% tenían dos hermanos, el 12,2% eran hijos únicos, el 5,5% tenían tres hermanos, y el resto (4,3%) más de cuatro hermanos. El nivel socioeconómico, determinado por la situación laboral de los padres y la ubicación del colegio en el que estaban escolarizados, era medio. Concretamente, en relación al nivel de estudios de los padres y madres de los participantes, la mayoría tenía estudios básicos (un 72,1% de los padres y un 59,2% de las madres), y en menor medida estudios medios (un 11,7% de los padres y un 10,6% de las madres) o estudios universitarios (un 4,8% de los padres y un 3,4% de las madres). Sobre el resto se desconoce el nivel educativo. Con respecto a la situación laboral, la mayoría de los padres estaban en situación activa (88,6% de los padres y el 73,2% de las madres). En la tabla I se presentan las características de la muestra total y de las tres submuestras que se establecieron en base a la categoría ponderal (normopeso, sobrepeso y obesidad). No se hallaron diferencias significativas entre las submuestras en ninguna de las variables sociodemográficas examinadas.

Instrumentos de evaluación

Variables sociodemográficas: los participantes completaron un breve cuestionario sociodemográfico proporcionando información sobre su edad, sexo, trabajo de su madre y padre, situación familiar, número de hermanos, y país de nacimiento.

Peso y talla: se midió la talla de los participantes descalzos utilizando un estatómetro portátil (Leicester Tanita

HR 001®; graduación: 1 mm) y se determinó el peso en una balanza digital (Beurer BF-100®; precisión: 100 g).

Índice de masa corporal (IMC) y clasificación ponderal (normopeso, sobrepeso y obesidad): se establecieron siguiendo los WHO Child Growth Standards, que tienen en cuenta el IMC, el sexo y la edad³⁴. El IMC se obtuvo con la fórmula peso/talla² (kg/m²). Siguiendo estas normas “sobrepeso” corresponde a +1 desviación estándar (D.E.) (equivalente a IMC de 25,4 kg/m² para hombres y de 25,0 kg/m² para mujeres a los 19 años) y “obesidad” a +2 D.E. (equivalente a un IMC de 29,7 kg/m² en ambos sexos a los 19 años)³⁵.

Hábitos de alimentación y actividad física: los participantes completaron un cuestionario construido para este estudio que incluía 14 ítems relativos a su alimentación (lugar donde comían; número de comidas habituales al día; frecuencia de ingesta de fruta, verdura y alimentos ricos en grasa y azúcares; percepción de su cantidad de ingesta de fruta y verdura respecto a niños de su misma edad) y actividad física (frecuencia de actividad física fuera del horario escolar y número de horas de actividad de ocio sedentaria al día). Algunos ítems eran de respuesta múltiple (e.g. *Señala las comidas que haces normalmente: desayuno, almuerzo, comida, merienda, cena y recena*), y en otros los sujetos tenían que responder valorando la frecuencia de su conducta en una escala que podía ir de *muchísima* a *muy poca*, de *nunca* a *todos los días* o de *mucha más* a *mucha menos*. (e.g. *¿Crees que comes más o menos fruta que la mayoría de niños de tu edad? Mucha más, algo más, la misma, algo menos o mucha menos*).

Procedimiento

La muestra de este estudio fue reclutada en varias aulas de 4º a 6º de educación primaria de siete colegios públicos y concertados de la provincia de Alicante, seleccionados al azar de zonas urbanas y rurales, de la costa y del interior. Tras solicitar la autorización a los directores de los centros y obtener el consentimiento informado de los padres, se realizó la evaluación de los participantes en las aulas de los propios colegios. El 95% de los padres dieron la conformidad para la participación de sus hijos en el estudio. Los participantes completaron los cuestionarios de forma anónima. Se distribuyeron los cuestionarios y se leyeron en voz alta las instrucciones. Se pidió a los participantes que contestaran con sinceridad y levantarán la mano si les surgía alguna duda. Ningún participante dejó más del 20% de los ítems sin responder, de modo que no se excluyó ningún cuestionario del análisis de datos. El Comité de Ética de la institución de la que forman parte los autores aprobó previamente el estudio.

Análisis estadísticos

Una vez los participantes completaron los cuestionarios, se llevó a cabo el análisis estadístico de los datos recogidos. Para la comparación de las variables cualitativas se utilizó la prueba Chi-cuadrado y para la compara-

Tabla I
Características de la muestra

Variables	Normopeso (n = 284)		Sobrepeso (n = 212)		Obesidad (n = 127)		Total (n = 623)	
	n	%	n	%	n	%	n	%
<i>Edad</i>								
10 años	68	23,9	48	22,6	28	22	144	23,1
11 años	134	47,2	120	56,6	60	47,2	314	50,4
12 años	82	28,9	44	20,8	39	30,7	165	26,5
<i>Sexo</i>								
Niñas	151	53,2	106	50	55	43,3	312	50,1
Niños	133	46,8	106	50	72	56,7	311	49,9
<i>Número de hermanos</i>								
Hijos únicos	27	9,5	30	14,2	19	15	76	12,2
1 hermano	180	63,4	130	61,3	76	59,8	386	62
2 hermanos	50	17,6	29	13,7	22	17,3	101	16,2
3 hermanos	17	6	11	5,2	6	4,7	34	5,5
4 ó más hermanos	10	3,7	12	5,6	4	3,2	26	4,3
<i>Origen</i>								
Español	241	84,9	179	84,4	115	90,6	535	85,9
Otros países	43	15,1	33	15,6	12	9,4	88	14,1
<i>Estudios del padre</i>								
Universitarios	13	4,8	12	5,9	5	4,2	30	4,8
Medios	33	12,2	28	13,7	12	10,2	73	11,7
Básicos	208	76,8	151	73,7	90	76,3	449	72,1
No lo sabe	17	6,3	14	7,8	11	9,3	42	6,7
<i>Estudios de la madre</i>								
Universitarios	12	4,4	7	3,4	2	1,6	21	3,4
Medios	28	10,2	25	12	13	10,7	66	10,6
Básicos	165	60	122	58,7	82	67,2	369	59,2
No lo sabe	70	25,4	54	26	25	20,5	149	22,9
Padre trabaja actualmente	254	46	191	34,6	107	19,3	552	88,6
Madre trabaja actualmente	205	44,9	154	33,7	97	21,2	456	73,2
<i>Estado civil</i>								
Casados	233	82	178	84	100	78,8	511	82,1
Separados/Divorciados	48	16,9	32	15,1	22	17,3	102	16,4
Padre/madre soltero/s	1	0,4	0	0	0	0	1	0,2
Huérfanos	2	0,7	2	0,9	5	3,9	9	1,4

ción de medias el análisis de varianza (ANOVA). El nivel de significación establecido fue $p < 0,05$. Se hallaron los tamaños del efecto de las diferencias que resultaron significativas. Todos los análisis fueron realizados mediante el paquete estadístico SPSS-19 para Windows.

Resultados

Prevalencia de obesidad, sobrepeso y normopeso, y diferencias de sexo, edad y nivel educativo de los padres

De la muestra total del estudio ($n = 623$), 212 participantes presentaron sobrepeso (34%) y 127 obesidad

(20,4%). El resto tenían un peso normal ($n = 284$; 45,6%). No se encontraron diferencias estadísticamente significativas ($\chi^2 = 3,41$, $p > 0,05$) respecto al sexo de los sujetos entre los que presentaron normopeso, sobrepeso y obesidad. En relación a la edad de los participantes, tampoco se hallaron diferencias estadísticamente significativas ($p < 0,05$) entre las categorías ponderales ni para el grupo del sexo masculino ($\chi^2 = 7,39$) ni para el del femenino ($\chi^2 = 4,38$). En el nivel educativo de los padres, las diferencias tampoco fueron estadísticamente significativas ($p < 0,05$) entre los niños con normopeso, obesidad o sobrepeso ($\chi^2 = 4,94$ para estudios del padre y $\chi^2 = 5,79$ para la madre de varones; $\chi^2 = 5,74$ para estudios del padre y $\chi^2 = 4,69$ para la madre de mujeres).

Con respecto a los hábitos de alimentación de los niños varones, se han encontrado diferencias estadísticamente significativas en las variables “*lugar donde comen habitualmente*” ($p < 0,05$), “*tomar desayuno habitualmente*” ($p < 0,05$) y “*tomar merienda habitualmente*” ($p < 0,01$). Los niños con normopeso comían con mayor frecuencia en el comedor escolar que los que presentaron sobrepeso y obesidad, que lo hacían con mayor frecuencia en su casa. Además, los niños con obesidad comían más a menudo en casa de sus abuelos que aquellos con sobrepeso y normopeso. Por otro lado, los niños con obesidad tomaban desayuno habitualmente en menor frecuencia que los que presentaron sobrepeso y normopeso. Lo mismo ocurre respecto a merendar habitualmente, con un menor porcentaje de los obesos que merendaba de forma habitual, seguidos de los que presentaron sobrepeso y en menor medida de los que tenían normopeso. No se encontraron diferencias estadísticamente significativas ($p < 0,05$) para el resto de las variables de alimentación. Respecto al ejercicio físico, se hallaron diferencias estadísticamente significativas ($p < 0,05$) en la variable “*hacer deporte fuera del horario escolar*”. Se encontró un mayor porcentaje de niños con normopeso que realizaba deporte casi todos los días, seguido de los que presentaron sobrepeso y obesidad. No se hallaron diferencias estadísticamente significativas en la variable “*número de horas de ocio sedentario diario (TV, videojuegos e internet)*”. En la tabla II se presentan los resultados de las comparaciones entre las variables de alimentación y ejercicio físico en el grupo del sexo masculino.

En las niñas sólo se encontraron diferencias estadísticamente significativas en las variables de alimentación “*tomar cena*” ($p < 0,005$) y “*tomar recena*” ($p < 0,01$) y en la variable de ejercicio físico “*número de horas de ocio sedentario diario (TV, videojuegos e internet)*” ($p < 0,05$). Se observó que las niñas con normopeso tomaban cena y recena en mayor porcentaje que las niñas con sobrepeso y obesidad. Por otro lado, la comparación de medias en el número de horas de ocio sedentario diario fue significativa entre el grupo de las niñas obesas y con sobrepeso. Las niñas con obesidad presentaron una media de horas de ocio sedentario diario mayor que las que tenían sobrepeso (tabla III).

Discusión

El exceso de peso es un problema muy prevalente en los niños de 10 a 12 años, alcanzando una tasa del 34% de sobrepeso y el 20.4% de obesidad según los resultados del presente estudio. Estos datos son superiores a los de trabajos previos que refieren tasas de obesidad que oscilan entre el 13% y el 19%, y de sobrepeso entre el 12,4% y el 26%^{2,27,29}. Los resultados no mostraron

diferencias estadísticamente significativas ($p < 0,05$) entre las tres categorías ponderales en las variables sexo, edad y nivel de estudios de los padres y madres. Este hallazgo es coherente con un estudio realizado en la provincia de Alicante que tampoco encontró diferencias respecto a estas variables²⁷. Sin embargo, no coinciden con los resultados de otros trabajos que indican prevalencias más altas de obesidad y sobrepeso en niños varones^{2,29} y en hijos de padres y madres con niveles educativos más bajos^{2,29,30}.

Con respecto a los hábitos de alimentación de los niños varones según su categoría ponderal, se han encontrado diferencias estadísticamente significativas en el lugar donde comen de forma habitual, así como en el hábito de tomar desayuno y merienda. En las niñas sólo se encontraron diferencias estadísticamente significativas en tomar cena y recena. Estos resultados podrían sugerir que los niños con normopeso realizan más comidas al día, lo que puede estar indicando, como el estudio de Toschke et al.³² señala, que la toma de pocas comidas al día podría suponer un factor de riesgo para la obesidad y el sobrepeso infantil. Por otro lado, en nuestro estudio se ha encontrado que los niños varones con normopeso comían habitualmente con mayor frecuencia en el comedor escolar que los que presentaron sobrepeso y obesidad, quienes lo hacían con mayor frecuencia en su casa y en casa de sus abuelos. Estos hallazgos respaldan los encontrados en los estudios de la AESAN²⁹ y Procter et al.³¹, que refieren que el comer en comedores escolares habitualmente puede ser un factor protector de la obesidad y sobrepeso infantil.

En referencia a la práctica de ejercicio físico, sólo se hallaron diferencias estadísticamente significativas en hacer deporte fuera del horario escolar para el grupo de los niños varones y en el número de horas de ocio sedentario diario para el grupo de niñas. Los resultados sugieren que los niños con normopeso realizan con mayor frecuencia ejercicio físico que los que presentan sobrepeso y obesidad, y que las niñas obesas utilizan más horas de ocio sedentario que las que presentan sobrepeso. Estos datos van en la línea de los encontrados en otros estudios^{29,33} que indican una mayor prevalencia de obesidad y sobrepeso en niños que realizan poca actividad física y hacen uso de más ocio sedentario.

Este estudio presenta una serie de limitaciones que deben atenderse, como el reducido número de colegios y localidades estudiadas que podría afectar a la representatividad de los resultados. Sería conveniente realizar estudios con muestras más amplias que confirmen estos datos y que analicen si existen diferencias en otras variables no estudiadas. A pesar de ello, debido a la escasez de estudios sobre obesidad y sobrepeso infantil y a la importancia del problema, estos datos, aunque tomados con cautela, deben ser tenidos en cuenta por la magnitud de las tasas de prevalencia de obesidad y sobrepeso que se han encontrado. Los resultados refuerzan la necesidad de desarrollar programas eficaces de prevención e intervención temprana para la obesidad infantil.

Tabla II
Diferencias en los hábitos de alimentación y práctica de ejercicio físico entre los niños varones de cada categoría ponderal

	Normopeso		Sobrepeso		Obesidad		χ^2
	n	%	n	%	n	%	
<i>Come fruta habitualmente</i>							
Muchísima	16	12,1	12	11,3	5	6,9	3,53
Mucha	36	27,3	28	26,4	16	22,2	
Ni mucha ni poca	62	47	53	50	41	56,9	
Poca	12	9,1	10	9,4	6	8,3	
Muy poca	6	4,5	3	2,8	4	5,6	
<i>Come fruta respecto a los niños de su edad</i>							
Mucha más	10	7,6	12	11,3	2	2,8	11,60
Algo más	26	19,7	27	25,5	20	27,8	
La misma	62	47	41	38,7	34	47,2	
Algo menos	29	22	23	21,7	10	13,9	
Mucha menos	5	3,8	3	2,8	6	8,3	
<i>Come verdura habitualmente</i>							
Muchísima	20	15,2	8	7,5	7	9,7	9,02
Mucha	13	9,8	22	20,8	14	19,4	
Ni mucha ni poca	48	36,4	35	33	23	31,9	
Poca	31	23,5	27	25,5	18	25	
Muy poca	20	15,2	14	13,2	10	13,9	
<i>Come verdura respecto a los niños de su edad</i>							
Mucha más	15	11,4	12	11,3	5	6,9	3,99
Algo más	20	15,2	23	21,7	17	23,6	
La misma	48	36,4	34	32,1	26	36,1	
Algo menos	31	23,5	25	23,6	15	20,8	
Mucha menos	18	13,6	12	11,3	9	12,5	
<i>Lugar de la comida</i>							
Casa	70	53	72	67,9	48	66,7	12,62*
Comedor	55	41,7	31	29,2	17	23,6	
Abuelos	5	3,8	3	2,8	6	8,3	
Otro lugar	2	1,5	0	0	1	1,4	
<i>Toma desayuno</i>							
Sí	128	97	92,5	98	62	86,1	8,38*
No	4	3	7,5	8	10	13,9	
<i>Toma almuerzo</i>							
Sí	118	89,4	91	85,8	63	87,5	0,69
No	14	10,6	15	14,2	9	12,5	
<i>Toma comida</i>							
Sí	129	97,7	104	98,1	72	100	1,59
No	3	2,3	2	1,9	0	0	
<i>Toma merienda</i>							
Sí	121	91,7	87	82,1	54	75	10,62**
No	11	8,3	19	17,9	18	25	
<i>Toma cena</i>							
Sí	117	88,6	89	84	60	83,3	1,52
No	15	11,4	17	16	12	16,7	
<i>Toma recena</i>							
Sí	34	25,8	15	14,2	13	18,9	5,17
No	98	74,2	91	85,8	59	81,9	
<i>Come bollería/golosinas</i>							
Todos los días	6	4,5	5	4,7	2	2,8	10,91
Algunos días	91	68,9	56	52,8	38	52,8	
Fines de semana	28	21,2	31	29,2	24	33,3	
Nunca	7	5,3	14	13,2	8	11,1	
<i>Hace deporte</i>							
Casi todos los días	99	75	70	66	38	52,8	18,29*
Algunos días	25	18,9	21	19,8	22	30,6	
Fines de semana	4	3	12	11,3	7	9,7	
Casi nunca	1	0,8	2	1,9	4	5,6	
Nunca	3	2,3	1	0,9	1	1,4	
	<i>M</i>	<i>DT</i>	<i>M</i>	<i>DT</i>	<i>M</i>	<i>DT</i>	<i>F</i>
Horas diarias de ocio sedentario (ver TV, videojuegos, internet)	2,55	1,54	2,56	1,61	3,03	1,72	2,37

*p < 0,05; **p < 0,01.

Tabla III
Diferencias en los hábitos de alimentación y práctica de ejercicio físico entre las niñas de cada categoría ponderal

	<i>Normopeso</i>		<i>Sobrepeso</i>		<i>Obesidad</i>		χ^2
	<i>n</i>	<i>%</i>	<i>n</i>	<i>%</i>	<i>n</i>	<i>%</i>	
<i>Come fruta habitualmente</i>							
Muchísima	15	9,9	18	17,1	10	18,2	11,54
Mucha	33	21,9	20	19	15	27,3	
Ni mucha ni poca	73	48,3	53	50,5	27	49,1	
Poca	21	13,9	8	7,6	3	5,5	
Muy poca	9	6	6	5,7	0	0	
<i>Come fruta respecto a los niños de su edad</i>							
Mucha más	6	4	6	5,7	2	3,6	7,43
Algo más	33	21,9	22	20,8	18	32,7	
La misma	78	51,7	58	54,7	27	49,1	
Algo menos	24	15,9	16	15,1	8	14,5	
Mucha menos	10	6,6	4	3,8	0	0	
<i>Come verdura habitualmente</i>							
Muchísima	11	7,3	13	12,3	5	9,1	10,59
Mucha	23	15,2	12	11,3	10	18,2	
Ni mucha ni poca	61	40,4	48	45,3	27	49,1	
Poca	28	18,5	20	18,9	11	20	
Muy poca	28	18,5	13	12,3	2	3,6	
<i>Come verdura respecto a los niños de su edad</i>							
Mucha más	6	4	5	4,7	4	7,3	5,86
Algo más	25	16,6	21	19,8	10	18,2	
La misma	57	37,7	45	42,5	24	43,6	
Algo menos	37	24,5	24	22,6	13	23,6	
Mucha menos	26	17,2	11	10,4	4	7,3	
<i>Lugar de la comida</i>							
Casa	78	51,7	67	63,2	32	58,2	8,20
Comedor	64	42,4	31	29,2	4	30,9	
Abuelos	8	5,3	7	6,6	17	7,3	
Otro lugar	1	0,7	1	0,9	2	3,6	
<i>Toma desayuno</i>							
Sí	140	92,7	92	86,8	51	92,7	2,91
No	11	7,3	14	13,2	4	7,3	
<i>Toma almuerzo</i>							
Sí	143	94,7	93	87,7	51	92,7	4,15
No	8	5,3	13	12,3	4	7,3	
<i>Toma comida</i>							
Sí	150	99,3	106	100	53	96,4	5,30
No	1	0,7	0	0	2	3,6	
<i>Toma merienda</i>							
Sí	136	90,1	90	84,9	48	87,3	1,56
No	15	9,9	16	15,1	7	12,7	
<i>Toma cena</i>							
Sí	137	90,7	90	84,9	43	72,8	5,81*
No	14	9,3	16	15,1	12	21,2	
<i>Toma recena</i>							
Sí	35	23,2	16	15,1	2	3,6	11,32**
No	116	76,8	90	84,9	53	96,4	
<i>Come bollería/golosinas</i>							
Todos los días	5	3,3	6	5,7	0	0	10,13
Algunos días	100	66,2	60	56,6	28	50,9	
Fines de semana	38	25,2	32	30,2	20	36,4	
Nunca	8	5,3	8	7,5	7	12,7	
<i>Hace deporte</i>							
Casi todos los días	57	37,7	39	36,8	22	40	3,37
Algunos días	54	35,8	38	35,8	21	38,2	
Fines de semana	18	11,9	13	12,3	7	12,7	
Casi nunca	17	11,3	9	8,5	3	5,5	
Nunca	5	3,3	7	6,6	2	3,6	
	<i>M</i>	<i>DT</i>	<i>M</i>	<i>DT</i>	<i>M</i>	<i>DT</i>	<i>F</i>
Horas diarias de ocio sedentario (ver TV, videojuegos, internet)	2,25	1,51	2,12	1,42	2,73	1,73	2,94*

*p < 0,05; **p < 0,01.

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Original / *Pediatría*

Cambios seculares antropométricos entre dos cohortes de niños sanos de 0 a 2 años de edad nacidos en 1993 y 2009

Teodoro Durá Travé^{1,2}, F. Gallinas Victoriano², E. Guembero Esarte², Noelia Ulibarrena Ascarza² y Grupo Colaborador de Navarra*

¹Departamento de Pediatría. Facultad de Medicina. Universidad de Navarra. ²Servicio de Pediatría. Complejo Hospitalario de Navarra. Servicio Navarro de Salud/Osasunbidea. Pamplona. España.

*Grupo Colaborador de Navarra: P. Aguirre Abad, P. Arnal Clemente, A. Barbadillo San Miguel, A. Díaz Alfaro, B. Erice Echegaray, V. Etayo Etayo, U. Flores Erro, C. Gurbindo Arana, B. Goñi Moreno, G. Grau Bolado, N. Gúrpide Ayarra, T. Hernández Lagunas, B. Larumbe Martin, JA. Heras Galindo, V. Leandro Liberato, Cl. Oteiza Orradre, J. Palau Bondía, R. Pelach Pániker, M. Ramos Zugasti, A. Roig Orts, F. Satrústegui Gamboa, L. Sota de la Gandara, M. Sota Virto, A. Vicondo Peña, C. Yoldi García, P. Zardoya Santos.

Resumen

Objetivo: Realizar un estudio antropométrico longitudinal en dos cohortes de niños sanos, desde el nacimiento hasta los 2 años de edad, nacidos en los años 1993 y 2009; analizándose los cambios seculares que pudieran haberse dado durante este intervalo de tiempo.

Material y métodos: Se han registrado retrospectivamente y comparado los pesos, tallas e índice de masa corporal (IMC) al nacimiento y a las edades de 3, 6, 9, 12, 15, 18 y 24 meses, de dos cohortes de niños sanos nacidos en los años 1993 (459 varones y 425 mujeres) y 2009 (460 varones y 481 mujeres).

Resultados: Los valores medios de los pesos e IMC de la cohorte del año 1993 eran significativamente superiores ($p < 0,05$) respecto a los de la cohorte del año 2009 a partir de los 6 meses de edad en las mujeres y de los 9 meses de edad en los varones y hasta los 24 meses de edad. En ambos sexos, no existían diferencias estadísticamente significativas entre los valores medios de las tallas registradas en cada una de las edades consideradas entre ambas cohortes.

Conclusiones: Al comparar los datos antropométricos entre dos cohortes de niños sanos nacidos en los años 1993 y 2009 en condiciones socio-sanitarias similares se ha advertido un “cambio secular” con sentido negativo en lo que respecta al peso e IMC, sin afectarse la talla.

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Palabras clave: Cambio secular del crecimiento. Índice de masa corporal. Lactante. Peso. Talla.

Correspondencia: Teodoro Durá Travé.
Complejo Hospitalario de Navarra.
Servicio de Pediatría.
31008 Pamplona. España.
E-mail: tduratra@cfnavarra.es

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ANTHROPOMETRIC SECULAR CHANGES AMONG TWO COHORTS OF HEALTHY INFANTS AGED 0-2 YEARS BORN IN 1993 AND 2009

Abstract

Objective: To accomplish a longitudinal anthropometric study in two different cohorts of healthy children (from birth to 2 years of age) who were born in 1993 and 2009. The possible appearance of secular changes within this period is analyzed.

Material and methods: Weight, height and body mass index (BMI) at birth and ages 3, 6, 9, 12, 15, 18 and 24 months in two different cohorts of healthy children born in 1993 (459 males and 425 females) and 2009 (460 males and 481 females) have been registered and analyzed.

Results: Average values for weight and BMI in 1993 cohort were significantly higher ($p < 0.05$) than those in 2009 cohort beyond 6 months of age in females and 9 months of age in males, up to 24 months of age. There were no statistically significant differences among average values of registered height in every period of age within both cohorts.

Conclusions: The comparison of anthropometric data among two different cohorts of healthy children born in 1993 and 2009 in similar social and health conditions shows a “secular change” in a negative sense regarding weight and BMI, without affecting height.

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Key words: Growth secular trends. Body mass index. Infant. Weight. Height.

Introducción

La aceleración secular del crecimiento hace referencia preferentemente a los cambios antropométricos observados en el último siglo en los países industrializados caracterizada por un incremento progresivo de la talla y/o peso junto a una aceleración de la maduración puberal, supuestamente relacionados con unas circunstancias socioeconómicas y sanitarias más favorables¹⁻⁷. Sin embargo, se han observado modificaciones antropométricas en sentido opuesto, bien coincidiendo con situaciones ambientales adversas, bien en poblaciones de distinto origen conviviendo en un mismo lugar y en parecidas condiciones, que han motivado que algunos autores prefieran utilizar el término “cambios seculares” ya que no prejuzga el sentido de las modificaciones.

La necesidad de actualizar las tablas de referencia para su adaptación a la tendencia secular del crecimiento explicaría la sucesión de estudios antropométricos llevados a cabo en diferentes poblaciones o comunidades nacionales y extranjeras en las últimas décadas^{2,8-15}. No obstante, los análisis comparativos de esta pléyade de estándares o patrones de referencia, en cuya elaboración se ha seguido distintas metodologías, han acabado prácticamente concluyendo que la elección de los patrones de referencia constituye un factor determinante en la valoración del crecimiento infantil¹⁶⁻²¹.

La valoración del crecimiento forma parte esencial de los exámenes periódicos de los programas de salud, y el registro e interpretación adecuados del peso, talla e índice de masa corporal son especialmente importantes durante los primeros años de vida (fase de crecimiento rápido), donde las desviaciones de los parámetros antropométricos serían especialmente sensibles a la privación de nutrientes y/o potenciales enfermedades subyacentes. Por tanto, convendría advertir los cambios seculares que pudieran sucederse en la primera infancia dada las consecuencias que se podrían derivar de una valoración antropométrica errónea a estas edades.

El objetivo del presente trabajo consiste en realizar un estudio antropométrico longitudinal en dos cohortes de niños sanos, desde el nacimiento hasta los 2 años de edad, nacidos en los años 1993 y 2009; analizándose los cambios seculares que pudieran haberse dado durante este intervalo de tiempo.

Material y métodos

El marco muestral considerado lo formaban los 4.688 (2.455 varones y 2.233 mujeres) y 6.844 (3.508 varones y 3.336 mujeres) nacidos en la Comunidad Foral de Navarra en los años 1993 y 2009, respectivamente (Instituto de Estadística de Navarra). Para calcular el tamaño de la muestra se ha tomado la hipótesis más desfavorable (0,50), una precisión del 0,03 para un grado de confianza del 95%, siendo el tamaño óptimo de 869 para los nacidos en el año 1993 y de 923 para los nacidos en el año 2009.

El programa institucionalizado de Atención a la Población Infantil en la Comunidad Foral de Navarra incluye exámenes periódicos de salud que permiten el registro en la historia clínica de los datos antropométricos (peso y talla) al nacimiento y a las edades de 3, 6, 9, 12, 15, 18 y 24 meses de cada paciente.

La muestra se obtuvo retrospectivamente mediante un muestreo estratificado proporcional a la distribución de la población infantil en las tres Áreas de Salud de Navarra: Pamplona (76,1%), Tudela (14,7%) y Estella (9,2%) (Censo de población, 2008. INE) que no ha variado en las últimas décadas. Para la obtención de submuestras correspondientes a cada Área de Salud, teniendo en cuenta que la población infantil atendida por cada uno de los pediatras de Atención Primaria en nuestra Comunidad es prácticamente similar, fue requerida de forma aleatoria la colaboración de 25 pediatras (18 del Área de Salud de Pamplona: 4 de la de Tudela y 3 de la de Estella). Estos profesionales debían revisar aleatoriamente las historias de 50 pacientes (25 niños y 25 niñas) que hubieran nacido en los años 1993 y 2009 y aportar los pesos y las tallas registrados al nacimiento y los 3, 6, 9, 12, 15, 18 y 24 meses de edad. Todos los pacientes tenían que ser de raza caucásica e hijos de padres caucásicos de origen español. Fueron excluidos aquellos pacientes que presentaban alguna enfermedad crónica conocida que pudiera condicionar su estado nutricional.

Se recibieron los datos antropométricos solicitados y debidamente cumplimentados de 884 (459 varones y 425 mujeres) y 941 (460 varones y 481 mujeres) pacientes nacidos en los años 1993 y 2009, respectivamente. De la totalidad de la muestra de nacidos en los años 1993 y 2009, 681 (77,1%) y 678 (72,1%) procedían del área de salud de Pamplona, 118 (13,3%) y 162 (17,2%) de la de Tudela y 85 (9,6%) y 101 (10,7%) de la de Estella, respectivamente.

La totalidad de los pacientes incluidos procedían de gestaciones únicas y embarazos a término de evolución normal, nacidos en el Complejo Hospitalario de Navarra de Pamplona, Hospital Reina Sofía de Tudela y Hospital García Orcoyen de Estella. Todas las mediciones (peso y talla) fueron realizadas por observadores cualificados, tanto en las maternidades de los hospitales como en las consultas de Pediatría de los Centros de Salud anteriormente referidos.

El peso y la longitud al nacer fueron valorados con el mismo material instrumental en cada hospital. El peso con una balanza digital Añó-Sayol, con un rango de lectura de 0,1 a 15 kg y una precisión de 10 g, en los propios paritorios; y la longitud con un tallímetro rígido inextensible Añó-Sayol con rango de lectura de 0 a 70 cm y precisión de 0,5 cm, en las primeras horas de vida.

Las valoraciones de peso y talla posteriores fueron realizadas en ropa interior, descalzos y en decúbito supino. El peso se midió con una báscula digital Añó-Sayol con rango de lectura de 0,1 a 15 kg y un margen de error de 10 g y la longitud con un tallímetro rígido

Tabla I
Distribución de la muestra obtenida por edades y sexo de ambas cohortes

Varones						
<i>Edad (meses)</i>	<i>1993</i>			<i>2009</i>		
	<i>N</i>	<i>Media</i>	<i>DE</i>	<i>N</i>	<i>Media</i>	<i>DE</i>
0	459	0,0	–	460	0,0	–
3	420	3,06	0,12	408	3,05	0,10
6	358	6,09	0,16	410	6,09	0,18
9	360	9,06	0,16	405	9,06	0,15
12	423	12,05	0,17	410	12,08	0,26
15	403	15,06	0,18	391	15,07	0,23
18	394	18,10	0,21	383	18,10	0,27
24	400	24,12	0,37	379	23,99	1,30

Mujeres						
<i>Edad (meses)</i>	<i>1993</i>			<i>2009</i>		
	<i>N</i>	<i>Media</i>	<i>DE</i>	<i>N</i>	<i>Media</i>	<i>DE</i>
0	425	0,0	–	481	0,0	–
3	390	3,06	0,12	405	3,05	0,12
6	341	6,11	0,15	431	6,12	0,18
9	319	9,08	0,16	411	9,06	0,13
12	373	12,05	0,18	401	12,07	0,20
15	353	15,08	0,21	396	15,07	0,20
18	369	18,06	0,22	377	18,10	0,26
24	375	24,12	0,40	397	24,07	1,06

inextensible Año-Sayol con rango de lectura de 0 a 90 cm y precisión de 0,5 cm.

El IMC se calculó según la fórmula: peso (en kilogramos) / talla² (en metros).

Los resultados se expresan como medias con sus intervalos de confianza (IC 95%). El análisis estadístico (t de Student) fue realizado mediante el programa informático *Statistical Packages for the Social Sciences* (SPSS) versión 20.0 (Chicago, Illinois, EE.UU.). La significación estadística fue asumida cuando el valor de *p* era inferior a 0,05.

Resultados

En la tabla I se expone la distribución por edades y sexo de la muestras obtenidas de ambas cohortes. No existían diferencias estadísticamente significativas entre los valores medios de las edades registradas entre ambos sexos y cohortes.

En la tabla II se exponen y comparan los valores medios de los pesos, tallas e índice de masa corporal correspondientes a cada una de las edades consideradas en las cohortes de varones nacidos en los años 1993 y 2009. Los valores medios de los pesos registrados en la cohorte del año 1993 eran significativamente superiores ($p < 0,05$) respecto a los de la cohorte del año 2009 desde los 9 hasta los 24 meses de edad. No existían diferencias estadísticamente significativas entre los

valores medios de las tallas registradas en cada una de las edades consideradas entre ambas cohortes. Asimismo, los valores medios de los índices de masa corporal calculados en la cohorte del año 1993 eran significativamente superiores ($p < 0,05$) respecto a los de la cohorte del año 2009 desde los 9 meses hasta los 24 meses de edad.

En la tabla III se exponen y comparan los valores medios de los pesos, tallas e índice de masa corporal correspondientes a cada una de las edades consideradas en las cohortes de mujeres nacidas en los años 1993 y 2009. Los valores medios de los pesos registrados en la cohorte del año 1993 eran significativamente superiores ($p < 0,05$) respecto a los de la cohorte del año 2009 desde los 6 hasta los 24 meses de edad. No existían diferencias estadísticamente significativas entre los valores medios de las tallas registradas en cada una de las edades consideradas entre ambas cohortes. Asimismo, los valores medios de los índices de masa corporal calculados en la cohorte del año 1993 eran significativamente superiores ($p < 0,05$) respecto a los de la cohorte del año 2009 desde los 6 hasta los 24 meses de edad.

En la figura 1 se exponen las diferencias de los valores medios de los pesos (en gramos) registrados al nacimiento y a las edades de 3, 6, 9, 12, 15, 18 y 24 meses, tanto de los varones como de las mujeres, entre las cohortes de nacidos en 1993 y 2009. Las diferencias en ambos sexos (510 gramos en varones y 390 gramos en mujeres) eran máximas a los 15 meses de edad.

Tabla II
Medidas antropométricas en los varones de ambas cohortes

Peso (kg) varones					
<i>Edad (meses)</i>	<i>Cohorte 1993</i>		<i>Cohorte 2009</i>		<i>p</i>
	<i>Media</i>	<i>IC 95%</i>	<i>Media</i>	<i>IC 95%</i>	
0	3,33	(2,89-3,77)	3,35	(2,93-3,77)	0,360
3	6,20	(5,60-6,80)	6,26	(5,57-6,95)	0,420
6	7,91	(7,17-8,65)	7,91	(6,95-8,87)	0,893
9	9,26	(8,37-10,15)	8,96	(7,96-9,96)	<0,001
12	10,26	(9,32-11,20)	9,84	(8,78-10,90)	<0,001
15	11,06	(9,97-12,15)	10,55	(9,45-11,65)	<0,001
18	11,69	(10,52-12,86)	11,24	(10,01-12,47)	<0,001
24	12,99	(11,65-14,33)	12,58	(11,20-13,96)	<0,001

Talla (cm)					
<i>Edad (meses)</i>	<i>Cohorte 1993</i>		<i>Cohorte 2009</i>		<i>p</i>
	<i>Media</i>	<i>IC 95%</i>	<i>Media</i>	<i>IC 95%</i>	
0	50,45	(48,54-52,36)	50,28	(48,49-52,07)	0,186
3	61,20	(58,99-63,41)	61,46	(59,14-63,78)	0,110
6	67,86	(65,85-69,87)	68,00	(65,70-70,30)	0,126
9	72,64	(70,55-74,73)	72,64	(70,34-74,94)	0,972
12	76,77	(74,36-79,18)	76,61	(74,10-79,12)	0,578
15	80,28	(77,64-92,92)	79,95	(77,20-82,70)	0,086
18	83,51	(80,86-86,16)	83,36	(80,40-86,32)	0,311
24	88,79	(85,54-92,04)	88,61	(85,51-91,71)	0,426

IMC (kg/m²)					
<i>Edad (meses)</i>	<i>Cohorte 1993</i>		<i>Cohorte 2009</i>		<i>p</i>
	<i>Media</i>	<i>IC 95%</i>	<i>Media</i>	<i>IC 95%</i>	
0	13,03	(11,76-14,30)	13,24	(11,99-14,49)	0,015
3	16,41	(15,05-17,77)	16,55	(15,16-17,94)	0,140
6	17,15	(15,83-18,47)	17,10	(15,59-18,61)	0,211
9	17,52	(16,12-18,92)	16,96	(15,54-18,38)	<0,001
12	17,41	(16,11-18,71)	16,87	(15,44-18,30)	<0,001
15	17,12	(15,84-18,40)	16,49	(15,22-17,76)	<0,001
18	16,75	(15,48-18,02)	16,18	(14,43-17,93)	<0,001
24	16,47	(15,13-17,81)	16,00	(14,73-17,27)	<0,001

Al comparar los datos obtenidos entre sexos, en ambas cohortes se observa como los valores medios de las tallas y de los pesos registrados así como de los índices de masa corporal calculados en cada una de las edades consideradas eran significativamente superiores ($p < 0,05$) en los varones. De hecho, en la cohorte de los nacidos en el año 1993 el peso medio de los varones superaba (en gramos) al de las mujeres en 140 al nacimiento, en 650 a los 12 meses y en 640 a los 24 meses; y la talla media de los varones superaba (en centímetros) a la de las mujeres en 0,81 al nacimiento, en 1,51 a los 12 meses y en 1,59 a los 24 meses. Mientras que en la cohorte de nacidos en el año 2009, el peso medio de

los varones superaba (en gramos) al de las mujeres en 140 al nacimiento, en 600 a los 12 meses y en 520 a los 24 meses; y la talla media de los varones superaba (en centímetros) a la de las mujeres en 0,85 al nacimiento, en 1,61 a los 12 meses y en 1,3 a los 24 meses.

Discusión

El objetivo básico del presente trabajo consistía en analizar los presumibles cambios seculares que pudieran haberse dado en el patrón de crecimiento entre dos cohortes de niños sanos, desde el nacimiento hasta los

Tabla III
Medidas antropométricas en las mujeres de ambas cohortes

Peso (kg) varones					
<i>Edad (meses)</i>	<i>Cohorte 1993</i>		<i>Cohorte 2009</i>		<i>p</i>
	<i>Media</i>	<i>IC 95%</i>	<i>Media</i>	<i>IC 95%</i>	
0	3,19	(2,81-3,67)	3,21	(2,77-3,65)	0,488
3	5,65	(5,01-6,29)	5,69	(5,07-6,31)	0,358
6	7,39	(6,65-8,13)	7,28	(6,57-7,99)	0,040
9	8,64	(7,78-9,50)	8,32	(7,51-9,13)	< 0,001
12	9,61	(8,57-10,65)	9,24	(8,33-10,15)	< 0,001
15	10,43	(9,28-11,58)	10,04	(9,00-1,08)	< 0,001
18	11,09	(9,83-12,35)	10,73	(9,65-11,81)	< 0,001
24	12,35	(10,82-13,88)	12,06	(10,84-13,28)	0,004

Talla (cm)					
<i>Edad (meses)</i>	<i>Cohorte 1993</i>		<i>Cohorte 2009</i>		<i>p</i>
	<i>Media</i>	<i>IC 95%</i>	<i>Media</i>	<i>IC 95%</i>	
0	49,64	47,84-51,44	49,43	(47,65-51,21)	0,186
3	59,84	(57,45-62,23)	59,85	(57,91-61,79)	0,110
6	66,46	(64,17-68,75)	66,61	(64,50-68,72)	0,126
9	71,00	(68,80-73,20)	70,81	(68,51-73,11)	0,972
12	75,26	(72,53-77,99)	75,00	(72,51-77,49)	0,578
15	78,87	(76,2-81,54)	78,65	(76,17-81,13)	0,086
18	82,12	(79,24-85,00)	81,90	(79,18-84,62)	0,311
24	87,20	(83,87-90,53)	87,31	(84,37-90,25)	0,426

IMC (kg/m²)					
<i>Edad (meses)</i>	<i>Cohorte 1993</i>		<i>Cohorte 2009</i>		<i>p</i>
	<i>Media</i>	<i>IC 95%</i>	<i>Media</i>	<i>IC 95%</i>	
0	12,95	(11,79-14,11)	13,12	(11,84-14,40)	0,038
3	15,76	(14,49-17,03)	15,88	(14,49-17,27)	0,205
6	16,75	(15,46-18,04)	16,41	(15,14-17,68)	< 0,001
9	17,13	(15,79-18,47)	16,58	(15,38-17,78)	< 0,001
12	16,96	(15,39-18,53)	16,46	(15,01-17,91)	< 0,001
15	16,74	(15,43-8,05)	16,30	(14,97-17,63)	< 0,001
18	16,38	(14,74-18,02)	16,03	(14,35-17,71)	0,004
24	16,21	(14,75-17,67)	15,81	(14,52-17,10)	< 0,001

2 años de edad, que prácticamente conformaban un intervalo generacional dado el periodo relativamente considerable que separaba sus años de nacimiento.

La mayoría de expertos, aunque algunos autores y/o instituciones hayan planteado recurrir a un único estándar o patrón de referencia internacional¹⁴, recomiendan la utilización de estándares de crecimiento nacionales o locales debido a la influencia que sobre el crecimiento tienen tanto factores étnicos y/o raciales como circunstancias ambientales (clima, hábitos dietéticos, condiciones socioeconómicas, culturales, etc.); y, además, siempre que sea posible con estándares obtenidos mediante estudios longitudinales en muestras representativas de la población a la que pertenece el niño sometido a estudio²². De hecho, este razonamiento fue lo que motivó a establecer como criterio de inclusión

que todos los participantes fueran de raza caucásica e hijos de padres caucásicos de origen español y, por tanto, quedaran excluidos los sujetos de otras etnias y razas que residieran en nuestra comunidad.

Sin embargo, en esta caso para comprobar si realmente existían diferencias seculares se compararon directamente los parámetros antropométricos (peso, talla e índice de masa corporal) registrados en ambas cohortes de niños nacidos en los años 1993 y 2009 y seguidos evolutivamente hasta los 2 años de edad; y no se utilizaron curvas y tablas de crecimiento previamente elaboradas ante la imposibilidad de disponer de unas curvas de crecimiento que pudieran servir de referencia común a ambas cohortes temporalmente tan distantes.

Los resultados obtenidos, tal y como era predecible, confirman en ambas cohortes un dimorfismo sexual

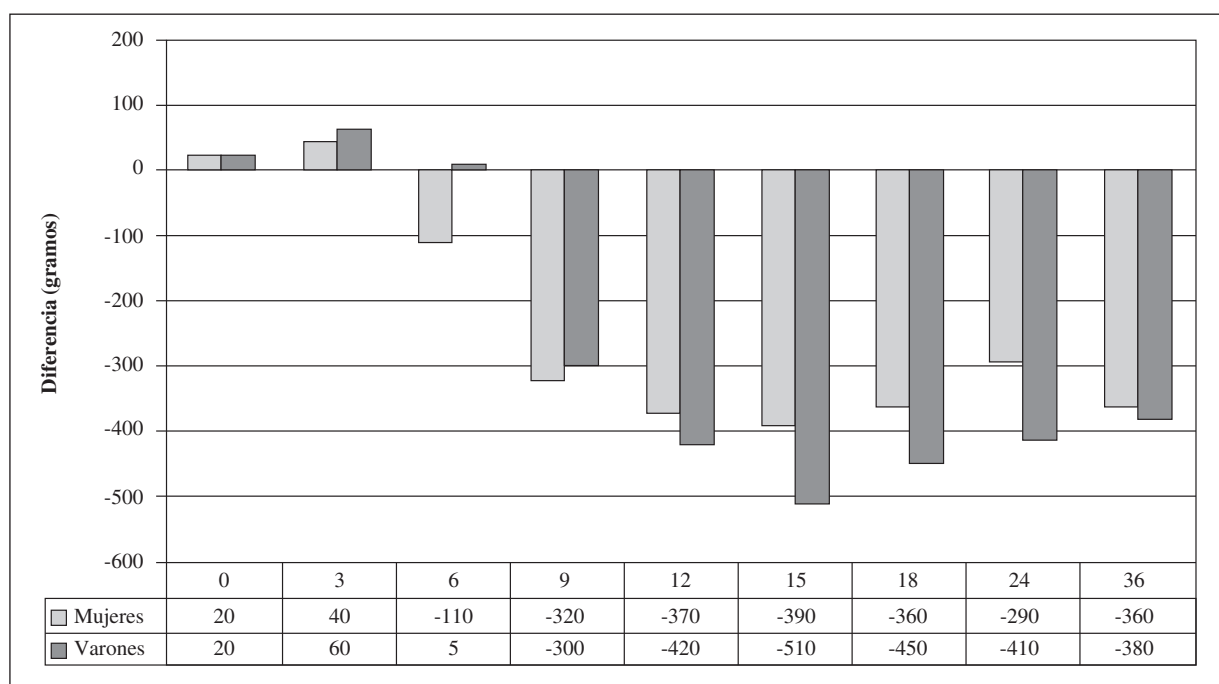


Fig. 1.—Diferencias de los valores medios de los pesos (en gramos), en varones y mujeres, entre ambas cohortes.

puesto de manifiesto desde el nacimiento y que iba incrementándose progresivamente a lo largo del periodo analizado; sin embargo, no se llegó a corroborar, en ambos sexos, una aceleración secular de los valores antropométricos (peso, talla e índice de masa corporal) en la cohorte de los nacidos en el año 2009 en relación con los de la cohorte de los nacidos en el año 1993. Es más, si bien no existían diferencias significativas entre los valores medios de las tallas entre ambas cohortes desde el nacimiento hasta los 2 años de edad, a partir de los 6 meses de edad en las mujeres y de los 9 meses de edad en los varones los pesos y los índices de masa corporal calculados eran significativamente inferiores en la cohorte de los niños nacidos en el año 2009.

Al considerar las diversas circunstancias cuya concurrencia pudieran haber diferenciado a ambas cohortes y, en consecuencia, podrían explicar las diferencias antropométricas registradas; se ha confirmado como la organización estructural y funcional del Sistema Navarro de Salud ha garantizado en ambas cohortes una asistencia sanitaria integral mediante los exámenes periódicos de salud y, en gran parte de los casos, con los mismos profesionales sanitarios. En este sentido, los protocolos de la Guía de actuación del Programa de Atención a la Población Infantil y Adolescente han proporcionado una homogeneidad en recursos humanos y materiales que avalan la uniformidad metodológica en las distintas actividades preventivas y de promoción de la salud (alimentación, vacunaciones, higiene, salud bucodental, etc.) en ambas cohortes. La única salvedad al respecto a tener en cuenta sería la de que en cada una de las cohortes analizadas se habían utilizado distintas curvas y tablas de crecimiento como

referencia; ya que mientras en la cohorte del año 1993 se habían utilizado las curvas y tablas de crecimiento longitudinales de la Fundación Orbeagoz cuyos datos antropométricos habían sido recogidos en el área metropolitana de la ciudad de Bilbao entre los años 1975 y 1988²³; en la cohorte del año 2009 las cartillas de salud incluían las referencias internacionales elaboradas por la OMS (*WHO Multicentre Growth Reference Study*, 2006) a partir de datos recogidos en seis países (Brasil, Ghana, India, Noruega, Omán y Estados Unidos) entre 1997 y 2003¹⁴.

En conclusión, al comparar dos cohortes de niños sanos nacidos en los años 1993 y 2009 en condiciones geográficas, climáticas, sociales y sanitarias aparentemente similares se ha advertido un “cambio secular” de signo negativo en lo que respecta al peso, sin afectarse la talla. Convendría que esta eventualidad pudiera ser confirmada mediante el diseño de estudios prospectivos que, a su vez, permitieran determinar sus causas.

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Original / Pediatría

New clinical practice guideline on enteral feeding in very low birth weight infants; first part

Tomás Sánchez-Tamayo^{1,2}, María G. Espinosa Fernández¹, María C. Moreno Algarra¹,
Verónica Fernández Romero¹, José Vallejo Triano¹, Elías Tapia Moreno¹ and Enrique Salguero García¹

¹Hospital Regional Universitario de Málaga. "Grupo multidisciplinar de investigación pediátrica". Unidad de Gestión Clínica de Neonatología. Málaga. España. ²Universidad de Málaga. Facultad de Medicina. Málaga. España.

Abstract

Introduction: The nutrition of very low birth weight (VLBW) infants is aimed at promoting a similar growth to that occurring in the uterus. However, in practice this is difficult to achieve and extrauterine growth restriction is frequent. The current tendency is to avoid this restriction by means of early parenteral and enteral nutrition. Nonetheless, uncertainty about many of the practices related with nutrition has resulted in a great variation in the way it is undertaken.

In 2009 and 2011 in our hospital there was an unexpected increase in necrotizing enterocolitis. To check to see whether our nutrition policy was involved, we undertook a systematic review and drew up clinical practice guidelines (CPG) about enteral feeding in VLBW infants. New considerations about the duration of the fortification and the use of probiotics have led to an update of these CPG.

Methods: A total of 21 clinical questions were designed dealing with the type of milk, starting age, mode of administration, rate and volume of the increments, fortification, use of probiotics and protocol. After conducting a systematic search of the available evidence, the information was contrasted and summarized in order to draw up the recommendations. The quality of the evidence and the strength of the recommendations were determined from the SIGN scale

Comment: These CPG aim to help physicians in their decision making. The protocolized application of well-proven measurements reduces the variation in clinical practice and improves results.

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Key words: Low birth weight infant. Prematurity. Necrotizing enterocolitis. Probiotics. Clinical practice guidelines. Evidence-Based medicine. Nutrition

Correspondence: Tomás Sánchez-Tamayo.
UGC de Neonatología 3ª planta.
Hospital Materno Infantil Carlos Haya.
Avenida Arroyo de los Ángeles, s/n.
Málaga. España.
E-mail: tomas.sanchez.tamayo@gmail.com

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NUEVA GUÍA DE PRÁCTICA CLÍNICA SOBRE NUTRICIÓN ENTERAL DEL RECIÉN NACIDO DE MUY BAJO PESO AL NACIMIENTO; PRIMERA PARTE

Resumen

Introducción: La nutrición de recién nacidos con peso muy bajo peso al nacer (MBPN) busca fomentar un crecimiento similar al que tiene lugar en el útero. Sin embargo, en la práctica, esto resulta difícil de conseguir y es frecuente encontrar una restricción del crecimiento extrauterino. La tendencia actual es evitar esta restricción por medio de una nutrición temprana parenteral y enteral. No obstante, la falta de certeza sobre muchas de las prácticas relacionadas con la nutrición ha dado lugar a una gran variación en los métodos.

En 2009 y 2011 en nuestro hospital se dio un aumento inesperado de enterocolitis necrosante. Para comprobar la posible implicación de nuestra política de nutrición, pusimos en marcha una revisión sistemática y redactamos unas directrices para la práctica clínica (DPC) sobre la alimentación enteral en recién nacidos con MBPN. Las nuevas consideraciones sobre la duración de la fortificación y el uso de probióticos han dado lugar a una actualización de estas DPC.

Métodos: Se definió un total de 21 preguntas clínicas sobre el tipo de leche, edad de inicio, modo de administración, porcentaje y volumen de los incrementos, fortificación, uso de probióticos y protocolo. Tras realizar una investigación sistemática de la evidencia disponible, la información fue contrastada y resumida para redactar las recomendaciones. La calidad de la evidencia disponible y la fuerza de las recomendaciones quedaron determinadas conforme a la escala SIGN.

Comentario: Estas DPC pretenden ayudar a los médicos en su toma de decisiones. La aplicación protocolizada de medidas bien probadas reduce la variación en la práctica clínica y mejora los resultados.

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Palabras clave: Recién nacido con bajo peso al nacer. Premadurez. Enterocolitis necrosante. Probióticos. Directrices para la práctica clínica. Medicina basada en la evidencia. Nutrición.

Introduction

Premature infants are born during what is a critical period for the growth and development of the nervous system. Nutrition for very low birth weight (VLBW) infants aims at promoting growth, similar to what takes places in utero, but without putting undue stress on metabolic and excretory functions. In practice this is difficult to achieve, not only because of difficulties posed by metabolic and digestive systems that are not fully developed, but also because of any intercurrent diseases an infant might have. In many cases the outcome is extrauterine growth restriction which often exacerbates prior intrauterine growth restriction.¹ Suboptimal nutrition during such a critical period can have irreparable consequences for growth and neurological development, and can cause diseases related to multiple metabolic syndrome to develop. The current trend is to avoid, wherever possible, extrauterine growth restriction through early, aggressive parenteral nutrition (with nutrients similar to those the foetus would receive through the placenta) and enteral feeding as early as possible.

At our hospital, in 2010 and 2011, we saw an unexpected increase in the incidence of necrotizing enterocolitis (NEC). The literature shows high variability in NEC rates among centres, and with practices relating to how enteral feeding is started and continued with. This variability has been described in different countries, hospitals, and even among health professionals within the same hospital. It can be explained by the large degree of uncertainty surrounding many of the procedures we perform on a daily basis.²

As such, we decided to write a clinical practice guideline (CPG) on VLBW feeding that might provide answers for questions mainly about type of milk, optimal time to start feeding, how to administer feeding, and rate and amount recommended when making increases. This guideline was presented orally at a neonatology conference³ and later in written form for the Paediatric Society of Eastern Andalusia.⁴

The first presentation did not include issues such as duration of fortification and whether or not probiotics are suitable—aspects which have led us to present the CPG, once updated, in a more complete manner.

The CPG is Split into two parts. Methodology and search strategy and the questions about the time of onset and type of milk is presented in first.

In the second part answers to the rest of questions presented in the guide are thoroughly addressed.

Scope & objectives of this guideline

This CPG is intended to help neonatologists make decisions about enteral feeding of VLBW infants in order to administer it safely and thus reduce the risk of NEC and postnatal growth restriction.

It addresses issues regarding type of milk, optimal time to start feeding, how to administer it, and rate and amount of increases. It also includes information on whether it is appropriate to continue fortification after hospital discharge or to use probiotics during the first weeks of life.

A second objective is to help reduce variability in daily practice among medical personnel.

Methodology

CPGs may be defined as recommendations that are systematically developed to help health professionals and patients make the right decisions in specific clinical situations. Implementing them may improve quality of care by reducing variability and by streamlining the process of adding and agreeing on the use of new advances in health care practices.

1) Development strategy

There are three possible strategies for developing a CPG:

- a) Perform an exhaustive search of the CPGs published on the subject in question and, when one of high quality is found, use it as a benchmark to adapt the CPG based on our answers.
- b) Develop a CPG *de novo*, based on analysing information obtained from randomized clinical trials (RCTs), meta-analyses, observational studies, and so forth.
- c) Use a “mixed” strategy, where we start by selecting CPGs and doing systematic quality reviews (SQRs) that will be used to adapt and update the clinical issues similar to our initial formulation. For issues that have not been previously addressed, the *de novo* strategy will be used.

We have used this approach in our case. The criteria for selecting CPGs were the score from the Appraisal of Guidelines for Research and Evaluation (AGREE) and a publication date after January 2007. As for systematic reviews, the selection criterion was based on critical reading, applying the Critical Appraisal Skills Program Español (CASPe) methodology.

After making the selection, we evaluated whether the CPG and SQR adequately responded to the questions formulated. To do this, we checked whether the following criteria were fulfilled:

- Consistency among the answers provided by the various CPGs.
- Whether these answers needed to be updated.
- Level of recommendation and applicability of them.
- Whether there were Cochrane reviews.

Table I
Levels of evidence and grades of recommendation according to the Scottish Intercollegiate Guidelines Network

Levels of evidence

1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with very low risk of bias.
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1-	Meta-analyses, systematic reviews of clinical trials, or clinical trials with high risk of bias.
2++	High-quality systematic reviews of cohort or case-control studies Cohort or case-control studies with very low risk of bias and a high probability of establishing a causal relationship.
2+	Well-conducted cohort or case-control studies with a low risk of bias and a moderate probability of establishing a causal relationship.
2-	Cohort or case-control studies with a high risk of bias and a significant risk that the relationship is not causal.
3	Non-analytical studies, such as case reports, case series or descriptive studies.
4	Expert opinion.

Grades of recommendation

A	At least one meta-analysis, systematic review, or RCT, rated as 1++ and directly applicable to the guideline's target population; or a body of evidence composed of studies rated as 1+ and with overall consistency among them.
B	A body of evidence composed of studies rated as 2++, directly applicable to the guideline's target population and demonstrating overall consistency among them; or evidence extrapolated from studies rated as 1++ or 1+.
C	A body of evidence composed of studies rated as 2+ directly applicable to the guideline's target population and demonstrating overall consistency among them; or evidence extrapolated from studies rated as 2++.
D	Level of evidence of 3 or 4; or evidence extrapolated from studies rated as 2+.

Good clinical practice

√	Recommendation of good clinical practice based on the clinical experience of the group that developed the guideline.
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- In addition, special emphasis was placed on analyzing the population and determining when each procedure was carried out and whether the result and subsequent recommendation was able to be extrapolated to other groups.

Depending on these criteria, it was decided whether the question was formulated *de novo* or whether it was updated. To do this, individual studies were used.

To grade the levels of evidence and strength of recommendations, the Scottish Intercollegiate Guidelines Network (SIGN) scale was used (table I).

2) Research, evaluation and selection of scientific evidence

The search was performed using a step-by-step approach. The inclusion criteria were:

- Documents written in any language.
- Published in the past 5 years.
- Focused on diagnosis and treatment.

Step No. 1

Search for position papers containing methodology for evidence-based medicine in order to update the guideline: Enteral feeding of VLBW infants.

The search was performed using synthesis tools: UptoDate licensed by the Andalusian Health e-Library (BV-SSPA), including the terms: enteral nutrition; premature infant. The “Approach to enteral nutrition in the premature infant” review and related topics were selected: “nutritional composition of human milk and preterm formula for the premature infant”, “human milk feeding and fortification of human milk for premature infants”, “breastfeeding the preterm infant”, and EBSCO’s DynaMed with the topic: feeding the premature infant.

Step No. 2

Search for previously drafted CPGs.

PubMed was searched using the following search protocol: ((“guideline”[Publication Type] OR “guidelines as topic”[MeSH Terms] OR “guidelines”[All Fields]) AND (“enteral nutrition”[MeSH Terms] OR “enteral nutrition”[All Fields])) AND (“infant, low birth weight”[MeSH Terms] OR “low birth weight infant”[All Fields]). Twenty (20) results were obtained, and no CPGs similar to the subject of the search were found.

We also searched specialized websites for CPGs: National Guideline Clearinghouse (NGC), CMA infobase, National Institute for Health and Clinical

Table II
Two examples of formulating PICO questions

<i>Patients</i>	<i>Intervention/comparison</i>	<i>Results</i>
VLBW infants < 32 GA and/or < 1,500 g	Keeping nil by mouth <i>versus</i> starting trophic enteral feeding in first 24 hours of life.	It has not been proven that fasting reduces the risk of NEC.
VLBW infants < 32 GA and/or < 1,500 g	Continuous enteral feeding <i>versus</i> intermittent feeding by bolus.	No benefits or disadvantages have been shown that enable continuous or bolus feeding to be recommended.

Excellence (NICE), Guía Salud and TripDatabase, and found one guideline fulfilling the search criteria: “Alimentación enteral del recién nacido menor o igual a 32 semanas de edad gestacional” published by the Mexican National Centre for Health Technology Excellence⁵. Based on this, two further guidelines were found, accessible online.^{6,7} Another was recently added.⁸ In addition, one CPG specifically for the prevention and management of NEC was found⁹.

Step No. 3

Search for systematic reviews and meta-analyses using the PubMed search filter for the terms “clinical queries/systematic reviews”, with a result of 12 articles. Search protocol on PubMed Clinical Queries: “enteral nutrition” AND “low birth weight”.

We also searched EMBASE using the term “systematic reviews” and obtained 7 results.

3) *Preparing the document and formulating questions*

Several health professionals were involved in preparing this document, and they practice at the Neonatal Unit of the Hospital Regional Universitario de Málaga. They were chosen based on experience in the field of neonatology and absence of conflicts of interest. In addition, the coordinator of the Carlos Haya Hospital Complex Integrated Training Unit took part as an expert in methodology, documentation, and development of literature-search protocols.

To formulate the key questions this guideline intends to answer, we used the PICO format—patient, intervention, comparison, and outcomes (examples of PICO-based questions can be found in table II)—addressing 21 questions in all (table III).

With regard to assigning level of evidence and degree of recommendation, we followed a peer evaluation done by different members of the team. In case of discrepancies, a new evaluation was performed by a third person in the research group.

Dr Carlos Sierra Salinas, who has been chair of the Spanish Society of Paediatric Gastroenterology, Hepatology, and Nutrition, and Dr Juana Guzmán Cabañas,

neonatologist at Hospital Reina Sofía and professor of paediatrics at the University of Cordoba, took part as external reviewers in research dedicated to premature infant nutrition¹⁰.

Discussion

Fasting or trophic enteral feeding?

NEC is a serious disease that is life-threatening and can cause serious after-effects. Prematurity and other factors that cause mesenteric ischemia have been associated with NEC (vascular redistribution in cases of intrauterine growth restriction, unstable haemodynamics, hypoxia, etc.). It usually occurs in premature infants who have already been fed through the gastrointestinal tract. For this reason, for many years high-risk children were made to fast; the thinking (with few evidence-based tests) was that by doing so, NEC could be prevented.

In addition, the early intake of food through the gastrointestinal tract favours its maturation and development. Given the challenge of improving gastrointestinal development and the risk of causing the onset of NEC, “trophic enteral feeding” (TEF) was opted for, which consists of providing minimal amounts of milk, maintaining the amounts for several days without increasing, or increasing them when tolerated but in a quantity which does not constitute a nutritional function (≤ 24 ml/kg/day). In clinical trials, TEF has been shown to have beneficial physiological and clinical effects on an individual basis: it improves tolerance, shortens the time to full enteral feeding, improves postnatal growth, and reduces cases of jaundice and sepsis.¹¹

The meta-analysis by Tyson¹² assessed the clinical effect of TEF in premature infants ≤ 33 weeks gestational age (GA) and with a birth weight of less than 1,500 g. It included 11 clinical trials that initiated TEF between the first and the eighth day of life, continuing it for 5-10 days. The control group was made to fast for the first 6-18 days after birth, though some could have water. The meta-analysis of the infants on TEF showed a decrease in total days needed to reach full enteral feeding (-2,6) and in hospital stay (-11,4) and in hospital stay. There was no increase in the figures for NEC ($n = 650$, $RR = 1.16$, $95\% CI = 0.75, 1.79$).

Table III

Twenty-one questions to be answered by the clinical practice guideline with regard to enteral feeding in infants less than or equal to 32 weeks gestational age and/or 1,500 g in birth weight

1. Should premature infants who have just born be nil by mouth or should trophic enteral feeding be started instead?
2. At what age after birth should feeding begin?
3. Are there particular situations where the start should be delayed?
 - 3.1. If breast milk is not available
 - 3.2. IUGR with no evidence of absent or reversed end-diastolic flow in the umbilical artery
 - 3.3. IUGR with absent or reversed end-diastolic flow in the umbilical artery
 - 3.4. Umbilical artery catheter
4. Which type of milk should be used to start feeding in premature infants who fulfil the above-cited characteristics?
5. Once feeding has been started, should trophic feeding be continued or should daily progressive increases be made?
6. What should the amounts and rate of increases in milk intake be?
7. What is the recommended method for administering feeding: bolus vs. continuous enteral?
8. Should we fortify breast milk?
9. In premature infants < 1,500 g, should fortification be continued after hospital discharge?
10. What would be the best approach to follow with regard to the use of fortifiers once the infant is breast-feeding directly?
11. Does standardizing the method of enteral feeding cause any benefit versus doing it based on a specific medical criterion?
12. Should the use of probiotics be recommended?
13. Should probiotics be used in all infants or only in those who are at risk and do not fulfil the exclusion criteria?
14. Should probiotics be used in infants who fulfil the criteria, regardless of whether they have been receiving antibiotics?
15. Should probiotics be used at all centres or only at those with a high rate of NEC?
16. How long should they be administered?
17. Administration of probiotics: Single strain versus multiple strains
18. What would be considered to be the most appropriate dose?
19. Should probiotics be administered only to infant formula or to any type of milk?
20. Prophylactic or therapeutic administration?
21. Can the administration of probiotics to premature infants be considered safe and effective?

Another meta-analysis from 2009 compared starting trophic amounts early on (prior to the 4th day of life and continued for 7 days) with fasting for the first week after birth, demonstrating that TEF was safe (no increased risk of NEC was found). However, none of the TEF-related physiological or clinical benefits shown in previous trials was found.¹³

Summary of the evidence

1+ In haemodynamically stable infants < 1,500 g, administration of amounts of milk less than 24 ml/kg/day, with no increases for one week, is as safe as fasting for the same period.

1+ TEF shortens the time needed to reach full enteral feeding, when compared with prolonged fasting.

Most of the studies included in the meta-analysis started feeding between the 2nd and 4th day and not in unstable children; hence the results cannot be extrapolated to all groups.

Recommendations

A Prolonged fasting should be avoided. Instead, trophic enteral feeding should be started in all haemodynamically stable infants < 1,500 g and/or < 32 weeks.

D Feeding should not be started in haemodynamically unstable infants.

When to start?

There is some controversy surrounding the optimal time to start enteral feeding. When trying to define it, the result is less divisive. The best evidence comes from a meta-analysis comparing feeding with progressive amounts early on (before the 4th day) versus starting later (from the 5th-7th day), with no statistically significant differences in incidence of NEC or mortality between the two groups.¹³ This meta-analysis has some significant limitations. It includes 5 trials

with a wide range of feeding regimens: two used TEF for 7 days before making the increases (making it impossible to discuss early enteral feeding). Eighty (80%) per cent of the patients included were small for their gestational age, and so the results could not be extrapolated to the proper weight results. (However, children with IUGR are at an increased risk of NEC compared with those who do not have IUGR and are of the same gestational age; thus the expected result would be better in those who are at the right weight.)

Henderson, in a multicentre case-control study of NEC risk factors, found no differences between the two groups with respect to the time to start feeding (2.9 days for the cases vs. 2.8 days for the control group).¹⁴

In our search strategy, we found no prospective studies addressing the start of enteral feeding from the first day of life. Most studies dealing with TEF include clinically and haemodynamically stable children who usually begin feeding on the second or third day. Thus the literature is oriented toward starting feeding in the first days of life, after the child is shown to be haemodynamically stable without vasoactive drugs. The availability of colostrum may be another criterion to consider in choosing the time to start feeding.

It has not been possible to demonstrate the safety of enteral feeding, neither with trophic amounts in unstable premature infants nor in those requiring inotropic drugs to maintain haemodynamics.

Summary of the evidence

1- There is no difference in the rate of NEC or gastrointestinal intolerance between starting feeding in the first four days (usually the 2nd to 4th day) or starting it after fasting for five days or more.

The group starting it early rarely begins on the first day of life. Most of the children included in the meta-analysis have IUGR. Haemodynamically unstable infants were excluded.

2++ Case-control studies have not shown that age at starting enteral feeding is a risk factor for NEC.

We found no trials that specifically address the issue of whether or not to start enteral feeding on the first day of life. It may indeed be possible in groups with a low risk of NEC, in particular if they are breast-fed.

Recommendations

B In premature infants, feeding should be started within four days, beginning as soon as they become haemodynamically stable (i.e., stable without vasoactive drugs).

√ Despite there is little evidence of starting feeding on the first day, we think that after the first few hours after birth, if the infant is hemodynamically stable and with good perfusion and skin color, the onset of trophic

feeding with colostrum or bank milk may have more benefits than risks. However, we cannot offer trials to support this assumption.

In certain situations, such as when breast milk is temporarily unavailable or for patients with IUGR or umbilical catheters, should the start of feeding be delayed?

In the literature we found no studies comparing the start of enteral feeding with formula until the mother's milk was available with temporary fasting until it was available. Since there is no clear evidence on the start time and the use of breast milk, the authors consider that before prescribing the start of formula feeding, colostrum should be obtained if possible, which is often already present from the first day in the mammary glands.

There is controversy around the optimal time to start enteral feeding in infants with IUGR. Most protocols recommend being very cautious with these children, delaying the start of feeding in most cases. The existing studies often include patients who are additionally associated with other risk situations, such as reversal of end diastolic flow in the umbilical artery. However, in a retrospective study with 578 infants with IUGR, with and without altered flow in the umbilical artery, Soregalori found no differences in NEC rates between the two groups¹⁵ (**evidence 2-**).

In a clinical trial that included only premature infants who were small for their gestational age and had an abnormal foetal Doppler ultrasound (absent or reversed end diastolic flow in the umbilical artery or evidence of foetal vascular redistribution), Leaf found no differences in NEC between groups that started feeding on the second day versus those who started on the sixth day¹⁶ (**evidence 1+**).

With regard to umbilical catheters, it might be plausible to think that blood flow in the gastrointestinal tract would be affected.

The clinical trial by Davey found no differences in the development of NEC among children with an umbilical catheter who started feeding on the second day of life (when the catheter was still in place) and those who started 24 hours after the catheter was removed (mean age: 5 days)¹⁷ (**evidence 1+**).

Boo¹⁸ et al. did a prospective cohort study to cast light on the risk factors of feeding intolerance. Starting feeding in the first 72 hours of life in patients with an umbilical catheter did not increase the risk (**evidence 2+**).

Summary of the evidence

2+ Children with IUGR and absent or reversed end diastolic flow in the umbilical artery had more NEC (OR: 2.13 CI: 1.49-3.03).

1+ In premature infants < 35 weeks with IUGR, pathological Doppler findings, and with no history of vasoactive drugs, starting enteral feeding during the 2nd day vs. the 6th day does not change the risk of NEC and shortens the time needed to reach full enteral feeding.

4 We found no evidence of the safety of starting feeding on the first day of life, nor in the presence of haemodynamic changes or those requiring vasoactive drugs.

1+ No relationship was found between umbilical catheter site and risk of developing NEC.

2+ In VLBW infants with an umbilical catheter, no relationship was found between catheter and digestive intolerance.

Recommendations

B In infants with IUGR < 35 weeks, with absent or reversed end diastolic flow in the umbilical artery, and with no haemodynamic changes or other gastrointestinal risk factors, feeding should be started during the 2nd day of life.

✓ We do not recommend starting feeding on day one, when vasoactive drugs are being given, when there are haemodynamic changes, or if poor skin perfusion is observed.

✓ If breast milk is not available on the second day, consider delaying the start until the third day.

C Patients with umbilical catheters should receive enteral feeding unless they have other risk factors contraindicating the early start of feeding.

What to use for feeding?

Various studies have shown donor breast milk to have a protective effect on NEC versus infant formula¹⁹ (**evidence 1++**). There are no trials comparing breast milk with formula². Fresh breast milk (not milk from the bank) reduces the rate of hospital-acquired infection. As such, the feeding of choice for premature infants is breast milk; if it is not available, we will use milk donated by the bank and, and finally infant formula for premature infants.

Summary of the evidence

1++ Infant formula leads to a higher risk of developing NEC than human milk from the bank.

Fresh breast milk (not milk from the bank) reduces the rate of sepsis compared with formula, and this beneficial effect is dose-dependent.

Recommendations

A Wherever possible, start enteral feeding with colostrum or breast milk.

A If it is not available, start with donated human milk (milk from the bank).

✓ If breast milk is temporarily not available, evaluate whether to delay starting enteral feeding for a few hours until it becomes available.

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Original / *Pediatría*

New clinical practice guideline on enteral feeding in very low birth weight infants; second part

María Gracia Espinosa Fernández¹, Tomás Sánchez-Tamayo^{1,2}, María C. Moreno Algarra¹,
Verónica Fernández Romero¹, José Vallejo Triano¹, Elías Tapia Moreno¹ and Enrique Salguero García¹

¹Hospital Regional Universitario de Málaga. "Grupo multidisciplinar de investigación pediátrica". Unidad de Gestión Clínica de Neonatología. Málaga. España. ²Universidad de Málaga, Facultad de Medicina. Campus de Teatinos. Málaga. España.

Abstract

Introduction: The nutrition of very low birth weight (VLBW) infants is aimed at promoting a similar growth to that occurring in the uterus. However, in practice this is difficult to achieve and extrauterine growth restriction is frequent. The current tendency is to avoid this restriction by means of early parenteral and enteral nutrition. Nonetheless, uncertainty about many of the practices related with nutrition has resulted in a great variation in the way it is undertaken.

In 2009 and 2011 in our hospital there was an unexpected increase in necrotizing enterocolitis. To check to see whether our nutrition policy was involved, we undertook a systematic review and drew up clinical practice guidelines (CPG) about enteral feeding in VLBW infants. New considerations about the duration of the fortification and the use of probiotics have led to an update of these CPG.

Methods: A total of 21 clinical questions were designed dealing with the type of milk, starting age, mode of administration, rate and volume of the increments, fortification, use of probiotics and protocol. After conducting a systematic search of the available evidence, the information was contrasted and summarized in order to draw up the recommendations. The quality of the evidence and the strength of the recommendations were determined from the SIGN scale.

Comment: These CPG aim to help physicians in their decision making. The protocolized application of well-proven measurements reduces the variation in clinical practice and improves results.

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Key words: Low birth weight infant. Prematurity. Necrotizing enterocolitis. Probiotics. Clinical Practice guidelines. Evidence-Based medicine. Nutrition.

Correspondence: María Gracia Espinosa Fernández.
UGC de Neonatología 3ª planta.
Hospital Materno Infantil Carlos Haya.
Avenida Arroyo de los Ángeles, s/n.
Málaga. España.
E-mail: mgespinosaf@gmail.com

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NUEVA GUÍA DE PRÁCTICA CLÍNICA SOBRE NUTRICIÓN ENTERAL DEL RECIÉN NACIDO DE MUY BAJO PESO AL NACIMIENTO; SEGUNDA PARTE

Resumen

Introducción: La nutrición de recién nacidos con peso muy bajo peso al nacer (MBPN) busca fomentar un crecimiento similar al que tiene lugar en el útero. Sin embargo, en la práctica, esto resulta difícil de conseguir y es frecuente encontrar una restricción del crecimiento extrauterino. La tendencia actual es evitar esta restricción por medio de una nutrición temprana parenteral y enteral. No obstante, la falta de certeza sobre muchas de las prácticas relacionadas con la nutrición ha dado lugar a una gran variación en los métodos.

En 2009 y 2011 en nuestro hospital se dio un aumento inesperado de enterocolitis necrosante. Para comprobar la posible implicación de nuestra política de nutrición, pusimos en marcha una revisión sistemática y redactamos unas directrices para la práctica clínica (DPC) sobre la alimentación enteral en recién nacidos con MBPN. Las nuevas consideraciones sobre la duración de la fortificación y el uso de probióticos han dado lugar a una actualización de estas DPC.

Métodos: Se definió un total de 21 preguntas clínicas sobre el tipo de leche, edad de inicio, modo de administración, porcentaje y volumen de los incrementos, fortificación, uso de probióticos y protocolo. Tras realizar una investigación sistemática de la evidencia disponible, la información fue contrastada y resumida para redactar las recomendaciones. La calidad de la evidencia disponible y la fuerza de las recomendaciones quedaron determinadas conforme a la escala SIGN.

Comentario: Estas DPC pretenden ayudar a los médicos en su toma de decisiones. La aplicación protocolizada de mediciones bien probadas reduce la variación en la práctica clínica y mejora los resultados.

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Palabras clave: Recién nacido con bajo peso al nacer. Prematuridad. Enterocolitis necrosante. Probióticos. Directrices para la práctica clínica. Medicina basada en la evidencia. Nutrición.

Introduction

Nutrition for very low birth weight (VLBW) infants aims at promoting growth, similar to what takes places in utero, but without putting undue stress on metabolic and excretory functions. In practice this is difficult to achieve. In many cases the outcome is extrauterine growth restriction which often exacerbates prior intrauterine growth restriction.¹ The current trend is to avoid, wherever possible, extrauterine growth restriction through early, aggressive parenteral nutrition (with nutrients similar to those the foetus would receive through the placenta) and enteral feeding as early as possible.

At our hospital, in 2010 and 2011, we saw an unexpected increase in the incidence of necrotizing enterocolitis (NEC). To check to see whether our nutrition policy was involved, we undertook a systematic review and drew up clinical practice guidelines (CPG) about enteral feeding in VLBW infants.

Methodology

Several health professionals were involved in preparing this document, and they practice at the

Neonatal Unit of the Hospital Regional Universitario de Málaga. In addition, the coordinator of the Carlos Haya Hospital Complex Integrated Training Unit took part as an expert in methodology, documentation, and development of literature-search protocols. Likewise people with strong experience in the field of nutrition took part as external reviewers.

To formulate the key questions, health professional crew, used the PICO format—patient, intervention, comparison, and outcomes. With regard to assigning level of evidence and degree of recommendation we used the Scottish Intercollegiate Guidelines Network (SIGN) scale (table I).

After search, evaluation and selection of available scientific evidence, the recommendations are drawn to answer the key questions. Methodology and search strategy are widely described in part one.

Results

A total of 21 clinical questions were formulated (table II). Those regarding the time of onset and type of milk were already discussed in the first part of the guide. In response to the rest, we have drafted the recommendations which are discussed below.

Table I	
<i>Levels of evidence and grades of recommendation according to the Scottish Intercollegiate Guidelines Network</i>	
<i>Levels of evidence</i>	
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with very low risk of bias.
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1-	Meta-analyses, systematic reviews of clinical trials, or clinical trials with high risk of bias.
2++	High-quality systematic reviews of cohort or case-control studies Cohort or case-control studies with very low risk of bias and a high probability of establishing a causal relationship.
2+	Well-conducted cohort or case-control studies with a low risk of bias and a moderate probability of establishing a causal relationship.
2-	Cohort or case-control studies with a high risk of bias and a significant risk that the relationship is not causal.
3	Non-analytical studies, such as case reports, case series or descriptive studies.
4	Expert opinion.
<i>Grades of recommendation</i>	
A	At least one meta-analysis, systematic review, or RCT, rated as 1++ and directly applicable to the guideline's target population; or a body of evidence composed of studies rated as 1+ and with overall consistency among them.
B	A body of evidence composed of studies rated as 2++, directly applicable to the guideline's target population and demonstrating overall consistency among them; or evidence extrapolated from studies rated as 1++ or 1+.
C	A body of evidence composed of studies rated as 2+ directly applicable to the guideline's target population and demonstrating overall consistency among them; or evidence extrapolated from studies rated as 2++.
D	Level of evidence of 3 or 4; or evidence extrapolated from studies rated as 2+.
<i>Good clinical practice</i>	
√	Recommendation of good clinical practice based on the clinical experience of the group that developed the guideline.

Table II

Twenty-one questions to be answered by the clinical practice guideline with regard to enteral feeding in infants less than or equal to 32 weeks gestational age and/or 1,500 g in birth weight

1. Should premature infants who have just born be nil by mouth or should trophic enteral feeding be started instead?
2. At what age after birth should feeding begin?
3. Are there particular situations where the start should be delayed?
 - 3.1. If breast milk is not available
 - 3.2. IUGR with no evidence of absent or reversed end-diastolic flow in the umbilical artery
 - 3.3. IUGR with absent or reversed end-diastolic flow in the umbilical artery
 - 3.4. Umbilical artery catheter
4. Which type of milk should be used to start feeding in premature infants who fulfil the above-cited characteristics?
5. Once feeding has been started, should trophic feeding be continued or should daily progressive increases be made?
6. What should the amounts and rate of increases in milk intake be?
7. What is the recommended method for administering feeding: bolus vs. continuous enteral?
8. Should we fortify breast milk?
9. In premature infants < 1,500 g, should fortification be continued after hospital discharge?
10. What would be the best approach to follow with regard to the use of fortifiers once the infant is breast-feeding directly?
11. Does standardizing the method of enteral feeding cause any benefit versus doing it based on a specific medical criterion?
12. Should the use of probiotics be recommended?
13. Should probiotics be used in all infants or only in those who are at risk and do not fulfil the exclusion criteria?
14. Should probiotics be used in infants who fulfil the criteria, regardless of whether they have been receiving antibiotics?
15. Should probiotics be used at all centres or only at those with a high rate of NEC?
16. How long should they be administered?
17. Administration of probiotics: Single strain versus multiple strains
18. What would be considered to be the most appropriate dose?
19. Should probiotics be administered only to infant formula or to any type of milk?
20. Prophylactic or therapeutic administration?
21. Can the administration of probiotics to premature infants be considered safe and effective?

Recommendations for clinical practice guideline

Should feeding be started with a trophic period or directly with gradual increases?

The beneficial role of TEF has been previously discussed. In animal studies, the lack of nutrients in the gastrointestinal tract as result of prolonged fasting, was associated with decreased intestinal growth, mucosal atrophy, delayed maturation of intestinal enzymes, changes in perfusion, decreased gastrointestinal permeability, and therefore, a higher risk of bacterial translocation. These same studies demonstrate how early enteral feeding leads to a two- to threefold increase in gastrointestinal mucosal mass. This trophic effect might be mediated by several growth factors, such as insulin, epidermal, and other peptides, all of which are found in human milk. We can conclude that early enteral feeding prevents gastrointestinal atrophy, appears to stimulate the maturation of the gastrointestinal system, and may improve feeding tolerance, especially when colostrum

and human milk are used. Hence the most appropriate strategy for starting successfully and afterwards increasing enteral feeding amounts would be to begin with “minimal or trophic enteral feeding.”

By contrast, rapidly increasing enteral feeding amounts might lead to an increase in NEC figures. Berseth conducted a trial comparing a group where TEF with breast milk or formula at 20 ml/kg/day for 10 days was administered, to a second group with daily increases of 20 ml/kg/day from the first day of feeding. This trial established criteria for stopping the study if differences in the rate of NEC were observed when performing intermediate evaluations. The study was stopped when 144 infants had been enrolled, after objectify a lower incidence of NEC in the group that continued with trophic enteral feeding (1/70 vs. 7/74). It should be noted that no statistical significance was reached with this number (RR = 0.14, 95% CI: 0.02; 1.07). The group that was fed with trophic amounts had to stay in the hospital longer, though there was no statistical significance.

One of the limitations of this study is that feeding was started very late, around 9 days, which does not seem to be the practice that is widely used these days.²

The multicentre case-control study by Henderson cited above, showed that making increases at a faster rate may act as a risk factor for developing NEC.^{2,3} (**evidence 2++**).

Summary of the evidence

1+ In VLBW infants < 32 weeks gestational age, who have undergone prolonged fasting, starting feeding with daily increases of 20 ml/kg increases the risk of NEC compared with giving trophic feeding without daily increases.

2++ The shortest duration of trophic feeding and a faster rate of increases are related to a higher rate of NEC.

Recommendations

B Increases in milk should be made after a trophic period that varies based on risk of NEC (usually from 5 to 7 days).

B In premature infants who have had a period of prolonged fasting, trophic feeding should be started, without increasing the amounts during the first days.

How should the amounts and rate of breast-milk intake be increased and by how much?

After progressive feeding has been started, the traditional rate of increasing it has been 20 ml/kg/day. Based on a recent meta-analysis comparing different amounts of increases after one week of TEF it may be increased by up to 30-35 ml/kg/day. We cannot generalize this recommendation to include infants who weigh less than 1,000 g, are extremely premature, have IUGR, or are on mechanical ventilation, because the meta-analysis included few patients with these characteristics. This study concluded that with these increases, full enteral feeding was reached early on and birth weight regained without increasing the risk of NEC, compared with smaller daily increases⁴ (**evidence 1+**).

Summary of the evidence

1+ Rapid increases (up to 30-35/ml/kg/day) achieve a reduction until full enteral feeding is reached and birth weight regained. There were no effects on NEC (relative risk = 0.90; CI 95%: 0.46; 1.77).

*The trials on which it is based are generally conducted with infants > 1,000 g, and so they cannot be extrapolated to extremely low birth weight infants.

*Increases were generally performed around the first week of life and after a trophic period, and so any

effect they might have if started in the first days is not known.

Recommendations

A After the “trophic feeding period”, daily increases of up to 30 ml/kg/day are to be made, while monitoring digestive tolerance.

C In infants < 1,000 g, there is no evidence of the safety of these amounts, and so the recommended increases are 10-20 ml/kg/day.

✓ We propose increases of 10-15 ml/kg, which are to be increased on an individual basis twice daily, in order to monitor tolerance.

*10 ml/kg every 12 hours in infants < 1,000 g or with > digestive risk (up to 20 ml/kg/day). *With this, 100 ml of milk/kg/day is reached by day 4 of the increases.*

*15 ml/kg every 12 hours in infants > 1000 g (up to 30 ml/kg/day). *With this, 100 ml of milk/kg/day is reached by day 3 of the increases.*

How to administer milk: bolus vs. continuous enteral?

Because of their immaturity, premature infants require tube feeding with nasogastric or orogastric tubes, which allow feeding to be done continuously or intermittently by bolus. Both methods can theoretically have benefits and risks. After comparing them, a Cochrane meta-analysis concludes that no recommendation can be established in that regard. Significant differences were found only in days needed to reach full enteral feeding (earlier by bolus), without observing differences in somatic growth, NEC incidence or hospital stay⁵ (**evidence 1+**).

Summary of the evidence

1+ There is no evidence of the benefit of either manner of administering enteral feeding (bolus vs continuous).

Recommendations

A No recommendation can be made for either type of feeding (bolus vs continuous).

Should we fortify breast milk?

To answer this question we will focus on a Cochrane meta-analysis⁶ which showed improved physical growth and head circumference in the short term. However, it showed no improvement in bone mineral content, probably because some of the tests included

phosphate supplements in the non-intervention group, considering it “unethical” to discontinue doing so. Nor is it conclusive with regard to long-term benefit, perhaps because there are few studies that prolonged follow-up. It does not appear to increase the incidence of serious adverse effects (NEC or death), although flaws in the studies make it difficult to rely on this statement.

Fortification improves short-term growth with no proven adverse effects. Composition and appropriate dosage still need to be established.

Summary of the evidence

1+ Breast milk fortification promotes short-term growth and has no adverse effects.

Recommendations

A Breast milk should be fortified for premature infants < 1,500 g or under 32 weeks.

In premature infants < 1,500 g, should fortification be continued after hospital discharge?

We found no strong evidence in this regard. Fortifying breast milk after discharge, whether by maintaining a preterm formula with mixed feeding, or with a human milk fortifier, does not seem to improve growth at one year of age. One study shows increased weight and bone mineral content, but not bone density,^{7,8} also observing that those not fortified ingest larger amounts of breast milk.

In addition, excessive catch-up growth during the period close to or after discharge has been linked to cardiovascular disease, hypertension, obesity, or type 2 diabetes in adulthood.

Amounts of approximately 200 ml of unfortified breast milk may be sufficient for adequate growth after discharge (not in the initial period), thus reducing the risk of excessive catch-up growth.

Summary of the evidence

1-Fortification after discharge does not improve long-term growth versus administration of amounts of 200 ml/kg/day of breast milk.

Recommendations

D We cannot establish a systematic recommendation for fortification following hospital discharge.

✓ Try to have them ingest large amounts of unfortified breast milk, while monitoring the growth chart and

efficacy of intake. If these amounts are not good, maintain fortification with smaller amounts of milk.

What would be the best approach to follow with regard to the use of fortifiers once the infant is breast-feeding directly?

To reiterate the argument above, fortification should be maintained until close to term, hospital discharge, or in any case until the premature infant can ingest approximately 200 ml/kg/day of unfortified breast milk. To this end, breast milk may be obtained; fortify it in two or three doses, and for the rest, breast-feed. Preterm formula would be maintained with mixed breast-feeding instead of term formula. Once sucking is clearly effective and after verifying adequate growth, we would discontinue this practice so as not to hinder the breastfeeding process.

Does standardizing the method of enteral feeding result in any benefit versus doing it based on a specific medical criterion?

In a systematic review and meta-analysis of observational studies, a reduction of 87% in the risk of NEC was found after the implementation of a standardized enteral feeding protocol. The individual results of these studies are also consistent (**evidence 2++**)⁸.

At least two studies that included practices such as TEF and breast milk fortification yielded similar results (**evidence 2-**)^{9,10}.

Summary of the evidence

2++ Standardizing the enteral feeding regimen with the maximum evidence to date may lead to a decreased incidence of NEC.

Recommendations

B In neonatology departments, the enteral feeding regimen for premature infants < 1,500 g and/or < 32 weeks should be standardized based on the latest evidence.

Is the use of probiotics effective and safe?

NEC remains one of the leading causes of death, especially in VLBW infants. When given prophylactically, probiotics may prevent NEC from developing by colonizing the gut with beneficial organisms—which in turn would prevent pathogens from colonizing it and thereby improve the maturation and barrier function of the intestinal mucosa—and by modulating the immune system. Increasingly, studies are advocating their administration to VLBW infants.

A Cochrane review published in 2011 by Alfaleh¹⁰ performed a meta-analysis of 16 clinical trials that included 2,842 children. This study concludes that oral administration of probiotics significantly reduces the incidence of severe NEC (stage II or higher) (RR 0.35; CI: 0.24-0.52) and mortality (RR 0.40; CI: 0.27-0.60), but not hospital-acquired infections (RR 0.90; CI: 0.76-1.07). None of the trials included reported systemic infections caused by probiotics.

Summary of the evidence

1++ The use of prophylactic probiotics reduces the risk of NEC and neonatal death, but not the risk of late-onset hospital-acquired infections. Clinical trials are consistent in these respects. The analysis of the variability among them, which is low, and the low rate of adverse effects puts the level of evidence at 1++ with a high grade of recommendation.

1+ They are equally effective and safe in premature infants with a birth weight of less than 1,150 g.

Recommendations

A Administer prophylactic probiotics to premature infants < 32 weeks gestational age and/or with extremely low birth weight who do not fulfil the exclusion criteria.

Should they be used at all centres or only at those with a high rate of NEC?

Individual studies have suggested that the potential benefit of probiotics is greater at centres with high rates of NEC, considering high rates to be more than 10%. However, studies by Linn in 2005 and 2008 repeatedly showed a reduction in NEC in the “probiotics” group regardless of the rate (1.1% vs. 5.3% with $p = 0.03$ and 1.8% vs. 6.5%, with $p = 0.02$ respectively), with a number needed to treat (NNT) of 24 and 21^{11,12}.

Summary of the evidence

1+ The beneficial effect “reflected” as relative risk remains similar at centres with lower rates of NEC (RR 0.38 vs. 0.32) or mortality (RR 0.36 vs. 0.35), compared to centres with higher rates. Logically, the NNT will be higher if the prevalence of NEC or neonatal deaths is lower at a given centre.

Recommendations

A It is recommended to use probiotics at centres with a high rate of NEC and at those with a low rate.

Should they be used in all patients or only in those who do not fulfil the exclusion criteria?

One of the main concerns with regard to the use of probiotics in premature infants is the possibility of developing sepsis associated with them. Though the protective effects of probiotics on mucosal integrity are well known, it is not known whether there is the potential for this integrity to be disrupted.

In addition, in case of changes in the intestinal barrier both pathogens as probiotics may be translocated and enter systemic circulation, thus causing sepsis.

To date, only six cases of sepsis associated with probiotics have been published, all in patients undergoing abdominal surgery (short bowel syndrome secondary to intestinal atresia, gastroschisis, omphalo-coele, and NEC) or heart surgery^{1,14,15}. No cases of sepsis associated with the use of probiotics have been described in clinical trials that have evaluated their use in premature infants, which as a whole includes more than 1,200 patients.^{16,17} In addition, pharmacovigilance data in countries where the use of probiotics is widespread have shown no evidence of an increased number of sepsis cases associated with probiotics.

Summary of the evidence

3 Most studies on the use of probiotics have been conducted in patients in situations where it was appropriate to start enteral feeding. There have been reports of infections caused by probiotic species in critically ill or haemodynamically unstable patients or those undergoing intestinal tract surgery or with heart disease, that compromised mesenteric blood flow.

Recommendations

D Administration is not recommended in critically ill patients or those with changes in intestinal mucosal integrity.

When should probiotics be administered, regardless of the use of antibiotics or otherwise?

The gastrointestinal tract of a healthy breast-fed premature infant is not colonized by *Bifidobacterium* and *Lactobacillus* until approximately the tenth day of life. In premature infants fed with formula, this colonization is less diverse, with approximately 50% of *Bifidobacterium*.

In premature infants, this colonization is delayed and may also be dominated by bacteria such as species of *Enterobacteriaceae* and species of *Clostridium*.

Because it is important that commensal flora colonize the gastrointestinal tract early on in premature

infants, it seems logical that supplements should be started as soon as possible^{18,19,20} before pathogens have the opportunity to start colonizing. Based on this, most investigators start them once the premature infants are ready to start enteral feeding. Clinical and haemodynamic stability are desirable in order to ensure the integrity of intestinal function and a minimal risk of food intolerance or translocation.

There is a significant association between pathogen colonization and the use of antibiotics.¹⁸ In addition, the use of antibiotics also destroys the commensal flora, and so the beneficial effect of probiotics will also be diminished during antibiotic treatment.

On this point the studies diverge: Guthmann²¹ et al. administered probiotics to premature infants < 32 weeks with a birth weight of < 1,500 g (who did not fulfil the exclusion criteria, usually from the second day of life and if they tolerated at least 2 cc of enteral feeding) starting the first day after discontinuing antibiotic treatment, and each time they received a series of the same, continuing with this for up to 14 days. Linn^{12,13} by contrast administered probiotics from the start of feeding, continuing with them regardless of the use of antibiotics, and discontinuing them only in case of sepsis, haemodynamic instability, or risk situations involving intestinal mucosal integrity. In no case were adverse effects reported.

Summary of the evidence

We found no trials that specifically analyze the ideal time to start using probiotics. Most started them after enteral tolerance began.

We found no studies evaluating the efficacy of probiotics administration during antibiotic treatment. But they have definitely been used, and have shown no added risk.

Recommendations

✓ Probiotics may be used from the start, maintaining them continuously except in cases of sepsis, ileus, or critical situations that put the premature infant's life at risk.

✓ When using antibiotics, it will be necessary to administer probiotics after completing the antibiotic treatment.

How long should they be administered?

We found no trials comparing different durations of use for probiotics.

The elimination of probiotic microorganisms in the stool usually disappears within 2 to 3 weeks of completing administration.^{18,19} As such, it seems that they should be continued while there is still the risk of digestive intolerance, developing NEC, or death.²⁰

Summary of the evidence

3 With regard to the results published and given the inverse relationship between gestational age and possibility of developing NEC, and all-cause mortality, it seems advisable to continue with probiotic supplements until 34 to 36 weeks corrected age, when the risk of these unfavourable results is reduced.

Recommendations

D Administer probiotics daily until 35 weeks corrected age or discharge.

Administration: Single strain versus multiple strains

Not all species of probiotics have proven effective, since not all act the same way. As the medical literature shows, the beneficial effects of a probiotic may be highly specific to that strain and may not be generalizable even to other strains of the same species. Although many studies have been carried out using a single strain, many investigators support the use of multiple strains in order to create conditions as similar as possible to those of a healthy child.¹⁴

An evaluation of the literature shows better results when two or more species of probiotics were administered with a single strain. However, we found no trials that compare the administration of one strain versus multiple ones, but only case series extracted from trials comparing them *versus* placebo.

Guthmann²¹ in his meta-analysis evaluating the prophylactic administration of probiotics in premature infants to prevent NEC, stratified and compared the results of several clinical trials that used one or multiple strains. It includes 11 trials, 4 of which used a single strain; 4 multiple strains; and 3 a specific combination of *L. acidophilus* + *Bifidobacterium spp*, which is the combination with the highest number of premature infants included and results published (499 and 488 premature infants in each trial arm) with an RR of 0.29 (0.15-0.56).

Summary of the evidence

1+ Clinical trials using multiple strains of probiotics prophylactically to prevent the development of NEC in premature infants have shown better results.

Recommendations

C Using a combination of probiotics that have been tested as effective versus a single strain is preferred.

✓ Use only species that have been shown to be effective and cause no adverse effects.

Should probiotics be administered only to infant formula or to any type of milk?

The overall beneficial effect has been shown both in children fed exclusively with breast milk (RR 0.31; 0.14-0.67) as with mixed breastfeeding (RR 0.38; 0.22-0.66) or exclusively with formula (23/146 vs. 10/157).

Summary of the evidence

1+ Probiotics reduce NEC and mortality regardless of the type of milk used.

Recommendations

A Probiotics should be administered regardless of the type of milk used.

What would be considered the most appropriate dose?

It seems reasonable to think that there should be an optimal dose for the probiotic to be able to survive and overcome the barriers posed by gastric acid, bile, and commensal flora, thus proliferating and colonizing the gastrointestinal tract. At present the optimal dosage is not known. The results published show efficacy with minimum doses of 10^6 - 10^7 colony-forming units (CFU).²²

Most studies use doses of 3×10^9 CFU in infants 32 weeks gestational age, with efficacy and no adverse effects observed.

Summary of the evidence

2++ The mean dose used in clinical trials with premature infants < 32 weeks gestational age, and which has proven effective and safe, is 3×10^9 CFU.

Recommendations

D Experts recommend starting with half the dose, 1.5×10^9 , while the amount of milk is low (less than 50-60 ml/kg/day) because there may be problems of high osmolarity, and in addition, there are theoretical risks of poor intestinal transit.

C Increase to 3×10^9 when larger amounts are reached.

Prophylactic or therapeutic administration of probiotics?

The beneficial effect of probiotics has been shown when they are administered prophylactically.

Therapeutic use in cases of NEC or ileus has not been tested and entails theoretical risks. The risk of probiotic translocation and, as a result, of sepsis, is greater in critically ill VLBW patients who are at a potential risk for loss of intestinal integrity. There are no data justifying the use of probiotics in cases of suspected acute disease.^{23,24,25}

Summary of the evidence

There are no data on the use of probiotics for critically ill premature infants.

3 Data extrapolated from clinical trials in critically ill adults, comparing administration of a probiotic versus placebo, have shown increased mortality in the probiotic group.

Recommendations

D A therapeutic recommendation for the use of probiotics in confirmed NEC and suspected sepsis or serious acute disease cannot be made.

Final comments

"The idea that a single method will work for all children in all cases is unrealistic." Although this quotation by Hany Aly, which refers to non-invasive ventilation, could be applied to enteral feeding of premature infants, it is also true that the application of standardized measures reduces variability in clinical practice and achieves better results.

We believe that in a stable VLBW infant with a good Apgar score and without vasoactive or aggressive respiratory support, early trophic feeding should be started (no more than 2nd-3rd day) with breast milk. Haemodynamically unstable infants should be made to continue fasting. After a trophic period (longer in infants at higher risk), proceed with daily increases of up to 30 ml/kg/day in older infants weighing 1,000 g, and more cautious increases in younger infants or those with risk factors for NEC. Breast milk should start to be fortified once amounts greater than 100-120 ml/kg/day have been reached. A combination of probiotics that have proven efficacy and safety should be administered, regardless of the milk used and the centre's rate of NEC, beginning with the start of enteral feeding.

Given the above-mentioned measures, where the use of breast milk has independently been shown to have more relevance and better evidence, every effort should be made to have breast milk available from the start. Because there is no clear evidence on the start and it already exists for the use of breast milk, feeding may be delayed until it is possible to have breast milk or milk donated from a bank.

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Original / Alimentos funcionales

Efecto sobre el neurodesarrollo y neuroprotección en pez cebra de un extracto polifenólico de huesos de aceituna

Ernesto Cortés Castell¹, C. Veciana Galindo², L. Torro Montell², E. Sirvent Segura², M. M. Rizo Baeza³ y V. Gil Guillén⁴

¹Departamento de Farmacología, Pediatría y Q. Orgánica. Universidad Miguel Hernández. Campus de San Juan. Alicante, España. ²Laboratorio de Biotecnología y Proyectos. Biopartner S.L. ³Departamento de Enfermería y Nutrición. Universidad de Alicante. ⁴Departamento de Medicina Clínica. Universidad Miguel Hernández. España.

Resumen

Objetivo: Determinar el efecto de un extracto polifenólico de hueso de oliva en el desarrollo del sistema nervioso y frente al daño inducido mediante la neurotoxina ácido kaínico, utilizando como modelo animal el pez cebra.

Material y métodos: Se analiza el efecto del extracto a la máxima dosis tolerada (100 mg/ml de polifenoles) sobre la actividad colinérgica en larvas de pez cebra (72 horas post-fertilización). Se utilizan únicamente huevos fecundados sin anomalías. Se incuban 6 huevos/pocillo en microplaca de 24 pocillos en 2 ml de agua con DMSO (0,1 %) a $26 \pm 1^\circ \text{C}$: a) neurodesarrollo: agua (control) y con 100 mg/ml de extracto, como ensayo; b) neuroprotección: agua y ácido kaínico (100 μM) (control) y con 100 mg/ml de extracto (ensayo). Todas las incubaciones por triplicado. A las 72 h se examinan y verifica ausencia de anomalías. Las larvas se homogeneizan y en los sobrenadantes se cuantifica actividad acetilcolinesterasa y concentración proteínas.

Resultados: La cantidad de proteína y apreciación morfológica es análoga en todos los ensayos, indicando mismo desarrollo. La acetilcolinesterasa en las larvas de pez, con el extracto polifenólico es del 162,2% (SD 44,2) respecto a controles (100% de actividad) ($p < 0,01$). Las larvas de pez tratadas con ácido kaínico y extracto polifenólico presentan el 140,1% (SD 22,0) de actividad, respecto a las incubadas únicamente con la neurotoxina (100%) ($p < 0,05$).

Conclusión: Los polifenoles extraídos de los huesos de aceituna producen incremento de actividad colinérgica durante el neurodesarrollo larvario en el pez cebra y protección frente a la neurotoxina ácido kaínico.

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Palabras clave: Polifenoles. Hueso oliva. Acetilcolinesterasa. Ácido kaínico. Pez cebra.

Correspondencia: Ernesto Cortés Castell.
Universidad Miguel Hernández.
España.
E-mail: ernesto.cortes@umh.es

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EFFECT ON ZEBRAFISH NEURODEVELOPMENT AND NEUROPROTECTION OF A POLYPHENOLIC EXTRACT OLIVE SEEDS

Abstract

Objective: To determine the effect of a polyphenolic extract from olive pit on the development of the nervous system as well as its effect on pain induced by the neurotoxin kainic acid, taking the zebrafish as the animal model.

Material and methods: We analyse the effect of the extract at the maximum tolerated dose (100 mg/ml of polyphenols) on the cholinergic activity in zebrafish larvae (72 hours post-fertilization). Only fecundated eggs with no abnormalities are used. 6 eggs/bowl are incubated in a 24 bowls microplate in 2 ml of water with DMSO (0.1 %) at $26 \pm 1^\circ \text{C}$: a) neurodevelopment: water (control) and 100 mg/ml of extract, as an essay; b) neuroprotection: water and kainic acid (100 μM) (control) and 100 mg/ml of extract (essay). All incubations are in triplicate. After 72 h, incubations are examined and checked for any abnormalities. Larvae are homogenized and acetyl cholinesterase activity and protein concentration in supernatants is quantified.

Results: The quantity of protein and the morphologic appreciation is similar in all the essays, showing a standard development. Acetyl cholinesterase in fish larvae, with the polyphenolic extract is 162.2% (SD 44.2) compared to controls (100% of activity) ($p < 0.01$). Fish larvae treated with kainic acid and polyphenolic acid show 140.1% (SD 22.0) of activity, compared to those only incubated with the neurotoxin (100%) ($p < 0.05$).

Conclusion: Polyphenols extracted from olive pit produce an increase in the cholinergic activity during the larvae neurodevelopment in the zebrafish as well as protection against the neurotoxin kainic acid.

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Key words: Polyphenols. Olive pit. Acetyl cholinesterase. Kainic acid. Zebrafish.

Introducción

Hace tiempo que se conoce que la ingesta de determinados nutrientes puede influir sobre determinadas funciones cerebrales, de forma decisiva durante el desarrollo perinatal, pero también en otras etapas de la vida, como en la etapa adulta y la tercera edad. De hecho, recientemente se ha demostrado la existencia de una programación fetal o neonatal de la salud en la etapa adulta, lo que implica que nunca se deben considerar las distintas etapas fisiológicas de forma aislada, sino relacionadas. Entre estos nutrientes están los ácidos grasos poliinsaturados n-3 (DHA) y compuestos antioxidantes naturales como los polifenoles, siendo importantes para la formación y desarrollo de las neuronas y otras células del SNC, pero también son claves en los adultos para la prevención de enfermedades neurodegenerativas. Diversos estudios realizados *in vitro*, en modelos animales y en humanos han demostrado que la suplementación con estos nutrientes se asocia a una mejora de la función cognitiva, que se refleja en una mejora del proceso de aprendizaje o la memoria en niños o a una prevención del declive en personas de la tercera edad.

Estos conocimientos han despertado un creciente interés por nuevos alimentos ricos en sustancias con capacidad neuroprotectora, que puedan contribuir a prevenir la incidencia de factores degenerativos desde la infancia y mitigar el impacto de enfermedades de carácter neurodegenerativo, que presentan un creciente índice de prevalencia en la edad madura.

Diversos mecanismos de acción se han propuesto para explicar la capacidad neuroprotectora de estas sustancias, entre ellos la acción antiinflamatoria, la modulación de vías de señalización intracelular, la modulación de la expresión de proteínas, la inhibición de las vías apoptóticas o la acción antioxidante¹.

Los antioxidantes pueden anular los efectos perjudiciales de los radicales libres en las células², así una dieta abundante en frutas y vegetales ricos en polifenoles y antocianinas proporciona un riesgo más bajo de contraer cáncer, enfermedades cardíacas y algunas enfermedades neurológicas³. Sugiriéndose que los compuestos presentes en estos alimentos pueden prevenir la neurodegeneración causada por el estrés oxidativo⁴.

Los estudios realizados sobre el desarrollo del SNC del pez cebra⁵ indican que a las 24 horas ya se aprecia la segmentación del cerebro y se han formado estructuras como el tubo neural, la notocorda y los somitos (precursores de músculo y esqueleto). A los cinco días de desarrollo se han formado órganos sensoriales como los ojos y los oídos. Asimismo, ha aparecido el corazón, el hígado, los riñones y el páncreas, además de que los sistemas circulatorio, digestivo y nervioso son perfectamente funcionales. En este momento el pez es capaz de responder a estímulos visuales, olfativos y mecánicos y comienza a nadar buscando alimento.

El objetivo es determinar el efecto de la suplementación de un extracto polifenólico de hueso de oliva en

fenómenos de neuroprotección frente a daño inducido mediante la neurotoxina ácido kaínico (KA) y su influencia en el desarrollo del sistema nervioso central (SNC), utilizando como modelo animal el pez cebra.

Material y métodos

Se ha utilizado como modelo experimental la larva de pez cebra (*Danio rerio*), analizando el efecto de la suplementación del extracto a la máxima dosis tolerada (MTD) de 100 mg/ml de polifenoles en larvas de 72 horas post-fertilización (hpf)⁶. El efecto sobre el neurodesarrollo se realiza mediante el cultivo de los huevos en presencia del extracto. El efecto neuroprotector del extracto se determina frente a una pérdida controlada de neuronas colinérgicas. Como marcador del estado general del sistema nervioso central, en ambos casos, se utiliza la actividad colinérgica.

Para la realización de los ensayos fueron utilizados únicamente aquellos huevos fecundados que no presentaron ningún tipo de anomalía externa (asimetrías, vesículas,...) o cuya membrana estaba dañada. Se transfirieron 6 huevos/pocillo a una microplaca de 24 pocillos en un volumen de 2 ml con los siguientes tratamientos:

Neurodesarrollo: Para analizar el posible efecto sobre el neurodesarrollo se incubaron los huevos en agua con DMSO (0,1%)(Sigma-Aldrich) y en este mismo medio adicionado con 100 mg/ml del extracto de polifenoles, a $26 \pm 1^\circ\text{C}$ durante 72 h.

Neuroprotección: Se utilizó el ácido kaínico como neurotoxina inductora de daño neuronal. Se incubaron los huevos en agua con DMSO (0,1%) y ácido kaínico (100 μM) y el mismo medio con KA y 100 mg/ml del extracto, a $26 \pm 1^\circ\text{C}$ durante 72 h. Transcurrido este tiempo, se examinaron las larvas determinando que el estado general de las mismas era correcto, sin ningún tipo de anomalías externas visibles. Todas las incubaciones se realizaron por triplicado.

Una vez finalizada la incubación y su control se cuantifico la actividad de acetilcolinesterasa (AChE) mediante el método Ellman modificado⁷. Se homogeneizaron mecánicamente las larvas, se centrifugo a 12.000 rpm durante 10 minutos y se midieron los niveles de AChE en cada muestra. El método está basado en la hidrólisis enzimática del sustrato acetiltiocolina ATCh, y la tiocolina liberada reacciona con el ácido 5,5'-ditiobis-2-nitrobenzoico (DNTB), dando lugar al ácido 5-tio-2-nitrobenzoico, compuesto de color amarillo con máximo de absorbancia entre 405 y 420 nm. de onda. La reacción se llevo a cabo añadiendo a cada pocillo de la microplaca 280 l de DTNB en buffer PBS 0.1M (pH 7,8), 10 μl del extracto enzimático (homogeneizado), iniciándose la reacción al agregar 10 μl de cloruro de acetiltiocolina. Inmediatamente, en un lector de microplacas se hicieron las lecturas de absorbancia. Se realizaron tres replicados y como blancos se utilizaron 3 pocillos por microplaca sustituyendo el homogenei-

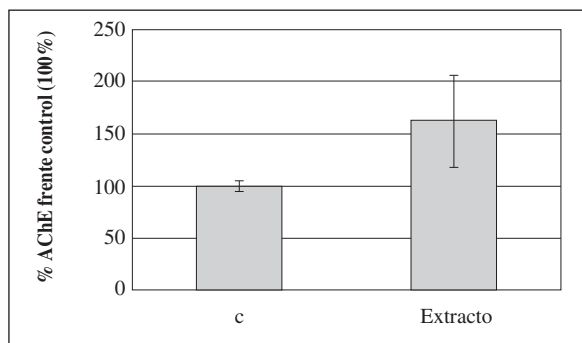


Fig. 1.—Niveles de acetilcolinesterasa (media $\pm$ SD) en las larvas de pez cebra incubadas con 100 mg/ml de extracto polifenólico de huesos de oliva, frente al control sin extracto, considerado como el 100% de actividad.

zado por buffer. Se realizó la recta de calibrado con 7 patrones entre 0-400 mU/ml de AChE, rindiendo una recta de $r^2 = 0,9735$ y de ecuación: AChE (mU/ml) = $116 \times \text{Abs}_{420\text{nm}}$.

Adicionalmente, se llevó a cabo la determinación de proteína total de cada grupo experimental con BCA⁸, para normalizar el efecto de los niveles de AChE con los niveles de proteína. El método de BCA emplea el ácido bicinconínico capaz de formar un complejo púrpura intenso con los iones Cu^+ en medio alcalino que tiene lectura de absorbancia a 562 nm. Se añaden 100 μl de BCA a 10 μl de muestra, se incuban 10 minutos a 60° C y se lee la absorbancia a 562nm. Se realizó la recta de calibrado con 10 patrones entre 0-1600 $\mu\text{g/ml}$, dando una recta de $r^2 = 0,9942$ y de ecuación: proteína ($\mu\text{g/ml}$) = $749 \times \text{Abs}_{562\text{nm}}$.

Resultados

La cantidad de proteína es análoga en todos los homogeneizados de las larvas de pez, siendo una buena medida del tamaño de las mismas y no constatándose diferencias ni efectos en los distintos medios de cultivo, al igual que la apreciación visual, sin alteraciones morfológicas visibles ni por acción del extracto de huesos de oliva, ni por el ácido kaínico.

a) Neurodesarrollo: Los niveles de acetilcolinesterasa en las larvas de pez cebra a las 72 hpf, en el medio de incubación con extracto de huesos de oliva ha sido del 162,2% (SD 44,2) frente a los controles únicamente con el agua con DMSO considerados el 100% de actividad, diferencia que es significativa según el test de Dunnett ($p < 0,01$). Esta diferencia se ilustra en la figura 1.

b) Neuroprotección: La actividad de acetilcolinesterasa en las larvas de pez cebra a las 72 hpf tratadas durante ese periodo con ácido kaínico en presencia del extracto de polifenoles es de 140,1% (SD 22,0) frente a la actividad de las que han sido incubadas únicamente con la neurotóxina que ha sido considerada el 100%, con una diferencia que es significativa según el test de

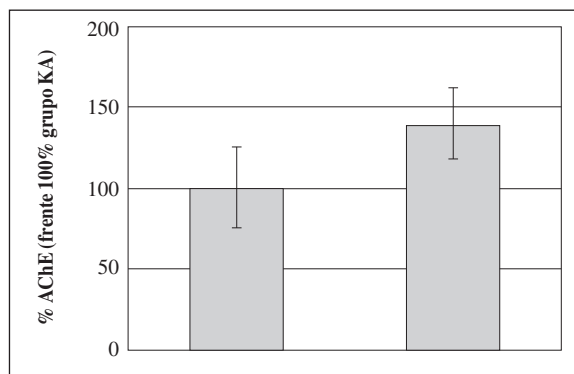


Fig. 2.—Niveles de acetilcolinesterasa (media y SD) en las larvas de pez cebra incubadas con 100 mg/ml del extracto y KA (100 μM), frente al grupo tratado únicamente con ácido kaínico, considerado como el 100% de actividad enzimática.

Dunnett ($p < 0,05$). Esta diferencia está ilustrada en la figura 2.

Discusión

El síndrome excitotóxico se ha descrito como una importante causa de daño y muerte neuronal en enfermedades neuropatológicas como la hipoxia, isquemia, epilepsia y la enfermedad de Alzheimer. Este fenómeno ha sido inducido en experimentos con roedores mediante la inyección de agonistas de glutamato como es el caso del ácido kaínico (KA), el cual causa *status epilepticus* junto con neurodegeneración posterior en la corteza y el hipocampo^{9,10,11}.

El modelo de pez cebra se ha utilizado en ensayos de excitotoxicidad⁵, observándose el mismo fenómeno que el descrito en el modelo murínico. A este respecto, el pez cebra (*Danio rerio*) se ha convertido en una buena herramienta para estudios neuroconductuales, ya que muestra neuropatologías y fenotipos conductuales que son cuantificables^{12,13} y propuesto como modelo experimental válido para estudio de la enfermedad de Alzheimer¹⁴. El pez cebra ofrece un compromiso razonable entre complejidad fisiológica y el rendimiento al tener un genoma caracterizado completamente, y mostrar homología fisiológica significativa a los mamíferos¹⁵, más estrechamente relacionado con los humanos que otros modelos como levaduras, gusanos o moscas, y el diseño y la conectividad en el centro de su sistema nervioso central (SNC) se correlaciona con la humana¹⁶. Su dualidad larva-adulto y disponibilidad de ambas formas es beneficiosa y permite la investigación de un espectro más amplio de fenómenos neurodegenerativos relacionados en la ontogénesis. Los embriones son transparentes y desarrollados externamente, hechos que permiten la observación directa de la embriogénesis y el desarrollo del sistema nervioso central. Los embriones son también fácilmente susceptibles a métodos para manipular los genes y la actividad de la proteína tales como la inyección de oligonucleótidos¹⁷, ARNm o cADN (transge-

nes), y para el cribado de bibliotecas de drogas están dispuestos en placas de microtitulación¹⁸. El desarrollo temprano del pez cebra permite analizar procesos y anomalías del sistema nervioso central, con una ventaja significativa en el análisis de las funciones cerebrales complejas características de los vertebrados¹⁹, con comportamientos de orden superior, incluyendo la memoria, respuestas condicionadas y comportamientos sociales como el aprender conductas²⁰ que lo hacen un modelo ideal para el estudio de trastornos del SNC²¹ y modelo para el estudio de efectos de agentes bioactivos, como el caso del presente estudio.

En el presente estudio se ha utilizado el ácido kaínico como neurotoxina inductora de daño neuronal en larvas de pez cebra, con el objetivo de estudiar las propiedades neuroprotectoras del extracto a estudio mediante la determinación de los niveles de acetilcolinesterasa (AChE) como marcador del estado general del sistema nervioso central. Para ello se ha analizado el efecto de la suplementación del extracto de polifenoles de huesos de oliva frente al daño neurotóxico en larvas de 72 horas post-fertilización (hpf) utilizando la máxima dosis tolerada del extracto⁶. El efecto neuroprotector se determinó frente a la pérdida controlada de neuronas colinérgicas, utilizado como marcador del estado general del sistema nervioso central. Los datos obtenidos muestran que el extracto incrementó los niveles de Acetilcolinesterasa de las larvas de pez cebra comparados con la actividad colinérgica en presencia de la neurotoxina, indicando un efecto protector de aproximadamente el 40%. Del mismo modo se constata un efecto beneficioso en el desarrollo del SNC del animal, al inducir un aumento en los niveles de la enzima, alcanzando un incremento del 62,2% respecto a los niveles observados en los controles.

Los polifenoles contenidos en los extractos procedentes del olivo presentan propiedades antioxidantes que hacen que sean candidatos para la investigación de enfermedades neurodegenerativas y reguladoras de la obesidad²². Además tienen otras actividades biológicas que le confieren importancia dentro de la “Dieta mediterránea”²³. Se ha demostrado, además de otros efectos beneficiosos, el poder protector de la ingesta de flavonoides, compuestos fenólicos contenidos en vinos, vegetales y frutas frente a la demencia²⁴.

Recientes estudios sugieren que los extractos del olivo inhiben la inflamación y reducen el estrés oxidativo, observado en ratas con una isquemia cerebral provocada²⁵. Su administración oral reduce el volumen de infarto, edema cerebral, la permeabilidad de la barrera sangre-cerebro, y mejora las puntuaciones de déficit neurológico después de la oclusión transitoria de la arteria cerebral media en ratas.

En otros estudios, se evaluó el posible efecto neuroprotector de extracto de hoja de olivo seco en la isquemia cerebral global transitoria en gerbos de Mongolia²⁶, valorando diferentes parámetros de estrés oxidativo y daño neuronal en el hipocampo y comparando con los efectos de la quercetina, un flavonoide conocido como

neuroprotector. El pretratamiento con extracto (100 mg/kg de peso del animal) inhibió significativamente la producción de superóxido y de óxido nítrico, disminuyó la peroxidación lipídica y aumento de actividad de la superóxido dismutasa, en todos los tiempos examinados. Además, ofreció mejoría histológica, observada por la disminución de daño neuronal en la región CA1 del hipocampo. Los efectos del extracto fueron significativamente mayores que los efectos de la quercetina (100 mg/kg peso del gerbo), indicando que ejerce una potente actividad neuroprotectora contra el daño neuronal en el hipocampo después de isquemia cerebral global transitoria, que puede atribuirse a sus propiedades antioxidantes.

Con este mismo extracto de polifenoles, se ha mostrado actividad antiinflamatoria en cultivo de monocitos humanos²⁷.

La mayoría de los estudios sobre los efectos de los polifenoles procedentes de extractos del olivo apuntan que su acción beneficiosa se debe a su capacidad antioxidante, causada por la capacidad de eliminar las especies reactivas de oxígeno y de nitrógeno implicadas en las enfermedades humanas¹.

Se concluye que los polifenoles extraídos de los huesos de aceituna producen un incremento de la actividad colinérgica durante el neurodesarrollo larvario en el pez cebra, así como una protección frente a la neurotoxina ácido kaínico.

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Original / *Alimentos funcionales*

Adherencia a la Dieta Mediterránea en futuras maestras

José Manuel Egeda Manzanera y Maximiliano Rodrigo Vega

Facultad de Educación. Departamento de Didáctica de las Ciencias Experimentales. Madrid. España.

Resumen

Introducción: La población universitaria española es vulnerable en sus hábitos alimentarios por diversas circunstancias. Esto implicaría en muchos casos el abandono de una dieta tradicional Mediterránea.

Objetivo: Determinar la adherencia a la dieta mediterránea (ADM) de una población universitaria de futura Maestras y analizar diversos factores que pudieran condicionar su calidad nutricional.

Material y métodos: Distribución del test Kidmed a una muestra de 212 universitarias con edades comprendidas entre 21 y 24 años. El índice Kidmed (de 0 a 12) indicaba si la ADM era baja (de 0 a 3), media (de 4 a 7) o alta (de 8 a 12). De cada encuestada se registraba edad, peso, talla e índice de masa corporal, así como la actividad física semanal. Para la comparación de los datos se han utilizado el test Chi cuadrado, la prueba Mann Whitney y ANOVA de un factor utilizando el programa estadístico SPSS 15.

Resultados: El 15,1% tenían un índice Kidmed bajo, el 60,4% intermedio y el 24,5% alto. La diferencia entre los diferentes grados de ADM y la situación nutricional (IMC) no existían diferencias significativas. Las diferencias entre aquellas alumnas que realizan actividad física (66%) y no (34%), respecto del índice Kidmed ($< 0,05$), eran debidas principalmente al desayuno (consumían más cereales y derivados y menos bollería).

Conclusiones: El 75,5% de las futuras Maestras necesitaban mejorar su ADM. En general, potenciar un desayuno de calidad y un mínimo de actividad física diaria serían dos aspectos nucleares en la mejora de hábitos. Sería conveniente establecer campañas educativas nutricionales para este tipo de población y máxime teniendo en cuenta su futura función social como educadores.

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Palabras clave: Dieta Mediterránea. Índice Kidmed. Universitarias. Actividad física.

ADHERENCE TO THE MEDITERRANEAN DIET OF FUTURE TEACHERS

Abstract

Introduction: The Spanish university population is vulnerable in their eating habits for various reasons. This would in many cases the abandonment of a traditional Mediterranean diet.

Objective: To determine the adherence to the Mediterranean diet (adm) of a university population of future Teachers and analyze various factors that may condition its nutritional quality.

Methods: Distribution Kidmed test to a sample of 212 university aged between 21 and 24. The Kidmed index (0-12) indicate whether the ADM was low (0 to 3), medium (4-7) or high (8 to 12). Each respondent was recorded age, weight, height and body mass index, and weekly physical activity. For comparison of the data was used Chi square test, the Mann Whitney test and ANOVA factor using SPSS 15.

Results: 15.1% had a low Kidmed index, 60.4% intermediate and 24.5% higher. The difference between the different levels of ADM is due to the consumption of fruits and vegetables ($p < 0.05$) mainly. Among the degrees of ADM and nutritional status (BMI) were not significantly different. The differences between those students who perform physical activity (66%) and no (34%) over the Kidmed index (< 0.05), were due primarily to breakfast consumed more cereals and cereal and pastries least).

Conclusions: 75.5% of future Teachers needed improved ADM. In general, enhance a quality breakfast and minimum daily physical activity would be two core aspects in improving habits. It would be appropriate to provide nutritional education campaigns for this population and especially considering their future social role as educators.

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Key words: Mediterranean diet. Kidmed Index. University. Physical activity.

Correspondencia: José Manuel Ejeda Manzanera.
Facultad de Educación.
Departamento de Didáctica de las Ciencias Experimentales.
C/ Rector Royo Villanova, s/n.
28040 Madrid. España.
E-mail: jmejeda@edu.ucm.es

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Abreviaturas

ADM: Adherencia a Dieta Mediterránea.

AF = Actividad Física.

DM = Dieta Mediterránea.

IMC = Índice de Masa Corporal.

Introducción

La dieta tradicional de los países mediterráneos se ha caracterizado por un alto consumo de cereales, frutas, verduras y hortalizas, legumbres, frutos secos y, especialmente, aceite de oliva; junto con un consumo moderado de pescados, huevos y productos lácteos, preferentemente yogur o queso, y un menor consumo de carnes y grasas animales¹⁻³. Todo ello, forma parte de la llamada dieta mediterránea (DM) que es probablemente uno de los modelos dietéticos más saludables que existen actualmente^{3,4}.

Por otra parte, la etapa en la cual un joven realiza los estudios universitarios suele coincidir con el momento en el que los estudiantes salen de su entorno familiar y se disponen a vivir de forma independiente, por lo que muchos de ellos se convierten por primera vez en los responsables de su alimentación. En este momento, los hábitos familiares se suelen abandonar debido a cambios en la organización de la vida, a recursos económicos limitados, a la gran oferta de comidas preparadas, a la comodidad o falta de tiempo o la inexperiencia en la compra, la planificación y la preparación de los alimentos⁵.

Todo esto justificaría, en gran medida, el estudio de la calidad de los hábitos alimentarios en la población universitaria utilizando para ello el modelo de DM. Es en esta población un momento especialmente vulnerable a la hora de conformar los hábitos alimentarios que van a influir en la salud y en la calidad de vida de estos jóvenes, en etapas posteriores de su vida. Además el centrar la investigación en un colectivo de Maestros en formación puede tener unas connotaciones muy interesantes de cara a conformar futuros agentes activos en salud pública.

Asimismo, la adhesión a la DM (ADM), como modelo alimentario saludable, puede cuantificarse mediante diferentes índices en los que se puntúa positivamente los alimentos y nutrientes que contribuyen beneficiosamente a proteger y preservar la salud⁶. Uno de estos índices es el cuestionario Kidmed, que permite determinar rápida y sencillamente el grado de ADM lo que, a su vez, permite identificar de manera inmediata poblaciones con hábitos alimentarios poco saludables y, por tanto, con riesgo de deficiencias y/o desequilibrios nutricionales⁵.

Este índice fue contrastado en varias poblaciones infantiles, adolescentes y juveniles españolas^{7,8-16} y europeas¹⁷⁻²².

Por otro lado, la práctica regular de actividad física (AF) se ha convertido en uno de los objetivos principales de los planes de salud pública debido a su relación

con la prevención de numerosas enfermedades crónicas. Numerosos estudios muestran una relación entre actividad física regular y enfermedad coronaria y cerebrovascular, arteriosclerosis, algunos cánceres, diabetes mellitus, salud ósea y depresión y ansiedad²³⁻²⁸.

En la población infantil y juvenil europea²⁹, el hábito de practicar ejercicio físico es bajo y disminuye al aumentar la edad, especialmente en las chicas^{30,31}.

En síntesis, el objetivo de este trabajo es conocer el grado de adhesión a la DM de la dieta de un grupo de universitarias madrileñas, futuras Maestras, y analizar diversos factores que pudieran condicionar su calidad nutricional (como el índice de masa corporal —IMC— o su actividad física), así como establecer las diferencias entre los distintos grados de ADM, para llegado el caso, ofrecer propuestas de mejora de su hábitos y de su situación nutricional.

Material y métodos

Se ha valorado la adherencia al patrón dietético mediterráneo aplicando el Test de Adhesión a la Dieta Mediterránea Kidmed³², a una muestra de 212 universitarias de la Facultad de Educación de la Universidad Complutense de Madrid, en el curso académico 2012/2013. Las edades de las participantes estaban comprendidas entre 21 y 24 años. El muestreo fue no probabilístico por conveniencia. Los motivos por los que todas las participantes fueron mujeres fueron porque la mayoría de las matrículas de las titulaciones estudiadas corresponden a mujeres.

La distribución de los cuestionarios y test Kidmed se realizó a través del campus virtual del alumnado de 4º curso previo consentimiento informado. De cada encuestado también se registraba la edad, las variables antropométricas (peso y talla) e índice de masa corporal, así como la actividad física. Antes de rellenar los cuestionarios, una persona cualificada explicó a las participantes cómo hacerlo y resolvió las dudas que surgieron durante su cumplimentación.

Aunque está documentado que los datos antropométricos declarados tienen un sesgo por la tendencia a infraestimar el peso y sobrestimar la talla, sin embargo existe una buena correlación entre datos reales y declarados, y dada la sencillez y economía de las mediciones, el peso y la talla autodeclarados son utilizados muy a menudo en estudios epidemiológicos³³⁻³⁵.

El índice de masa corporal (IMC) se calculó mediante la fórmula: $\text{Peso (kg)}/\text{Talla (m}^2\text{)}$. Según el valor del IMC se definieron cuatro grupos: (1) Bajo peso, si era inferior a 18,5. (2) Normalidad, si oscilaba entre 18,5 y 24,99. (3) Sobre peso, si oscilaba entre 25 y 29,99. (4) Obesidad, si era superior a 30.

El test Kidmed³² consta de 16 preguntas que deben responderse de manera afirmativa/negativa (sí/no). Las respuestas afirmativas en las preguntas que representan un aspecto positivo en relación con la dieta mediterránea (son 12) suman 1 punto, y las respuestas afirmati-

vas en las preguntas que representan una connotación negativa en relación con la dieta mediterránea (son 4) restan 1 punto. La puntuación total obtenida da lugar al índice Kidmed, que se clasifica en tres categorías:

- De 8 a 12: Dieta Mediterránea óptima (adherencia alta).
- De 4 a 7: necesidad de mejora en el patrón alimentario para adecuarlo al modelo mediterráneo (adherencia media).
- De 0 a 3: dieta de muy baja calidad (adherencia baja).

Para analizar la actividad física (AF) se utilizó un cuestionario en el que se preguntó si realizaba alguna actividad física con una duración superior a 30 minutos, el tipo de actividad y de cuántos días a la semana la realizaba.

Los resultados se analizaron estadísticamente mediante el paquete estadístico SPSS 15. Se realizó un análisis descriptivo de los datos, expresándose las variables cuantitativas como medias y desviaciones típicas y las variables cualitativas se describieron mediante frecuencias. Se utilizó el ANOVA de un factor para contrastar las medias del IMC respecto de los grados de adhesión a la DM. Para el estudio del contraste entre promedios de la puntuación total del test Kidmed se utilizaron pruebas no paramétricas (U de Mann-Whitney) debido a la distribución no normal de los datos. El test chi-cuadrado se utilizó para contrastar las proporciones entre las variables cualitativas (porcentajes de respuestas a los ítems del test Kidmed). La significación estadística se calculó al 95% de probabilidad.

Resultados

Característica de la muestra

La muestra estaba formada por 212 mujeres, alumnas de 4º curso de Grado de Magisterio. Las edades de las participantes estaban comprendidas entre 21 y 24 años, con una edad media de $21,4 \pm 0,8$. Los valores obtenidos para las medidas antropométricas eran: Peso-kg ($57,8 \pm 8,5$); Estatura-cm ($165,5 \pm 5,4$) e IMC-kg/m² ($21,2 \pm 2,8$).

Estado nutricional y adhesión a la Dieta Mediterránea

En cuanto a la clasificación porcentual de esta muestra universitaria la mayoría son normopeso (67,9%), hay un cierto porcentaje de universitarias con problemas de sobrepeso (12,3%) y bajo peso (19,8%). No se presenta ningún caso de obesidad.

Se determinó el IMC para los tres grados de adhesión a la DM (tabla I) observándose que los valores medios del IMC se encuentran en el rango del normo-

Tabla I
Distribución de valores medios* del IMC (kg/m²) en relación al grado de ADM

Baja adhesión (media $\pm$ DE)	Media adhesión (media $\pm$ DE)	Alta adhesión (media $\pm$ DE)
21,0 $\pm$ 2,5	21,2 $\pm$ 2,9	20,9 $\pm$ 2,6

*ANOVA de un factor $p < 0,05$ (puntuación total Kidmed). NS.

peso y, las diferencias no resultaron estadísticamente significativas (NS).

En la tabla II, se observa que el 15,1% de la totalidad de la muestra ($n = 212$) tenía un índice Kidmed bajo, un 60,4% intermedio y un 24,5% alto; siendo el valor medio del índice Kidmed de $5,90 (\pm 2,4)$, es decir, que un 75,5% de las universitarias necesitan mejorar su patrón alimentario.

Los ítems con una respuesta mayor con connotaciones positivas son el 11, 13, 2, 5, 7, 3 y 9, es decir: uso de aceite de oliva (98,1%), desayunar un lácteo (88,7%), consumir una primera pieza de fruta o zumo natural (80,2%), consumir pescado (69,8%), el gusto por las legumbres además de consumirlas (68,9%), toman verduras frescas una vez al día (66,0%) y el desayunar un cereal o derivado (63,2%). Asimismo entre los de menor respuesta estarían el 8, 10, 4 y 2, es decir: consumo de frutos secos y pastas y/o arroz (22,6%), así como la toma de una segunda verdura ó pieza de fruta (26,4% y 38,7% respectivamente).

Los ítems con una respuesta mayor con connotaciones negativas son el 14, 6, 16 y 12, es decir: consumo de bollería industrial (56,6%), acudir a un centro de comida rápida (29,3%), tomar golosinas o refrescos azucarados (11,3%) y no desayunar (10,4%).

Se estudió, para los grupos ponderales de IMC (bajo-peso, normopeso y sobrepeso), el grado de adhesión a la DM así como las respuestas obtenidas para los 16 ítems del test Kidmed. En la tabla III se exponen y comparan el grado de adherencia a la dieta mediterránea (índice Kidmed) en relación con el tipo de situación nutricional y, los porcentajes de los resultados del test Kidmed. En general no existen diferencias estadísticamente significativas entre los diferentes grupos de estado nutricional respecto de los diferentes grados de adhesión a la DM.

En cuanto a la puntuación total del test Kidmed (tabla III) obtenemos que las mujeres con bajo peso presentan un índice mayor ($6,3 \pm 2,4$) con respecto al resto de grupos ($5,8 \pm 2,5$ —normopeso— y $5,8 \pm 1,6$ —sobrepeso—) pero sigue sin establecerse diferencias estadísticamente significativas entre los grupos.

En síntesis, si nos fijamos en el grupo mayoritario, representado por las futuras Maestras con normopeso (el 67,9% del total de la muestra, $n=212$) dentro de ellas, las que tienen alta adherencia a la DM son un 25%, con lo que se evidencia que un porcentaje importante del resto de mujeres de este grupo (el 75%) debería modificar sus hábitos, tratando de aproximarlos a los patrones de la DM.

Tabla II
Porcentajes y puntuación al Test Kidmed (n = 212)

<i>Índice Kidmed</i>	<i>Media</i>	<i>Desv. estándar</i>	
Puntuación total	5,9	± 2,4	
<i>Grado de Adhesión a la DM</i>	<i>Total</i>	<i>IC-95%</i>	
Alta 8-12 ptos. (%)	24,5	16,3	32,7
Media 4-7 ptos. (%)	60,4	51,1	69,7
Baja ≤ 3 ptos. (%)	15,1	8,3	21,9
<i>% de Respuestas Kidmed</i>	<i>Total</i>	<i>IC-95%</i>	
1. Toma 1 fruta o un zumo natural todos los días	80,2	72,6	87,8
2. Toma una 2ª pieza de fruta todos los días	38,7	29,4	48,0
3. Toma verduras frescas una vez al día	66,0	56,0	74,2
4. Toma verduras frescas más de una vez al día	26,4	18,0	34,8
5. Consume pescado (por lo menos 2-3 veces a la semana)	69,8	61,1	78,5
6. Acude 1 vez o mas a la semana a un centro de comida rápida	29,3	19,7	36,9
7. Le gustan las legumbres y las toma más de 1 vez a la semana	68,9	61,1	78,5
8. Toma pasta y/o arroz casi a diario (5 días o más a la semana)	22,6	14,6	30,6
9. Desayuna un cereal o derivado todos los días (pan,...)	63,2	55,0	73,2
10. Toma frutos secos (al menos 2-3 veces a la semana)	22,6	14,6	30,6
11. Se utiliza aceite de oliva en casa	98,1	95,5	100
12. No desayuna	10,4	4,6	16,2
13. Desayuna un lácteo (yogurt, leche,...)	88,7	82,7	94,7
14. Desayuna bollería industrial, galletas o pastelitos	56,6	46,2	65,2
15. Toma dos yogures y/o 40 g de queso cada día	44,3	34,8	53,8
16. Toma golosinas, refrescos azucarados varias veces al día	11,3	5,3	17,3

IC = Intervalos de Confianza.

Tabla III
*Test Kidmed en relación a los grupos ponderales del estado nutricional y pruebas estadísticas**

<i>Índice Kidmed</i>	<i>Bajo peso n = 42</i>	<i>Normopeso n = 144</i>	<i>Sobrepeso n = 26</i>
Puntuación total (media ± DE)	6,3 ± 2,4	5,8 ± 2,5	5,8 ± 1,6
<i>Grado de Adhesión a la DM</i>			
Alta 8-12 ptos. (%)	28,6	25,0	15,4
Media 4-7 ptos. (%)	52,4	59,7	76,9
Baja ≤ 3 ptos. (%)	19,0	15,3	7,7
<i>% de Respuestas Kidmed</i>			
1. Toma 1 fruta o un zumo natural todos los días	95,2	76,4	76,9
2. Toma una 2ª pieza de fruta todos los días	42,9	36,1	46,1
3. Toma verduras frescas una vez al día	80,9	61,1	69,2
4. Toma verduras frescas más de una vez al día	33,3	20,8	46,1
5. Consume pescado (por lo menos 2-3 veces a la semana)	66,7	70,8	69,2
6. Acude 1 vez o mas a la semana a un centro de comida rápida	28,6	29,2	30,8
7. Le gustan las legumbres y las toma más de 1 vez a la semana	71,4	68,1	69,2
8. Toma pasta y/o arroz casi a diario (5 días o más a la semana)	19,0	25,0	15,4
9. Desayuna un cereal o derivado todos los días (pan,...)	61,9	63,9	61,5
10. Toma frutos secos (al menos 2-3 veces a la semana)	28,6	23,6	7,7
11. Se utiliza aceite de oliva en casa	100	97,2	100
12. No desayuna	9,5	11,1	7,7
13. Desayuna un lácteo (yogurt, leche,...)	95,2	86,1	92,3
14. Desayuna bollería industrial, galletas o pastelitos	57,1	55,6	61,5
15. Toma dos yogures y/o 40 g de queso cada día	47,6	43,1	46,1
16. Toma golosinas refrescos azucarados varias veces al día	14,3	9,72	15,4

*Prueba U-Mann-Whitney $p < 0,05$ (puntuación total Kidmed). NS. *Prueba Chi cuadrado con corrección de Bonferroni $p < 0,05$ (grado de adhesión a la DM y % de respuestas Kidmed). NS.

Tabla IV
Test Kidmed en relación a los grupos ponderales del grado de Adhesión a la DM

Ítem	Test Kidmed	% Alta (n = 52)	% Media (n = 128)	% Baja (n = 32)
1	Toma 1 fruta o un zumo natural todos los días	100,0 ^{bc}	82,8 ^{ac}	43,7 ^{ab}
2	Toma una 2ª pieza de fruta todos los días	80,8 ^{bc}	31,2 ^{ac}	6,2 ^{ab}
3	Toma verduras frescas o cocinadas 1 vez al día	96,1 ^{bc}	64,1 ^{ac}	25,0 ^{ab}
4	Toma verduras frescas o cocinadas > 1 una vez al día	61,5 ^{bc}	17,2 ^a	12,5 ^a
5	Consume pescado (por lo menos 2-3 veces a la semana)	84,6 ^c	76,6 ^c	25,0 ^{ab}
6	Acude $\geq$ 1 vez a la semana a un centro de comida rápida	7,7 ^{bc}	32,8 ^a	43,7 ^a
7	Las legumbres las toma más de una vez a la semana	80,8	68,7	56,2
8	Toma pasta y/o arroz (5 días o más a la semana)	19,2	23,4	25,0
9	Desayuna un cereal o derivado todos los días (pan,...)	84,6 ^c	65,6 ^c	18,7 ^{ab}
10	Toma frutos secos (al menos 2-3 veces a la semana)	38,5 ^c	20,3	6,2 ^a
11	Se utiliza aceite de oliva en casa	100,0	98,4	100,0
12	No desayuna todos los días	3,8 ^c	7,8 ^c	31,2 ^{ab}
13	Desayuna un lácteo (yogurt, leche,...)	96,1 ^c	93,7 ^c	62,5 ^{ab}
14	Desayuna bollería industrial, galletas o pastelitos	11,5 ^{bc}	68,7 ^a	81,2 ^a
15	Toma dos yogures y/o 40 g de queso cada día	76,9 ^{bc}	35,9 ^a	25,0 ^a
16	Toma golosinas o refrescos azuc. Varias veces al día	0,0 ^c	10,9 ^c	31,2 ^{ab}

^{a,b,c}Prueba Chi cuadrado con corrección de Bonferroni ($p < 0,05$): existen diferencias estadísticas significativas con respecto al superíndice (a, b y c).

En los tres grupos ponderales de IMC se observó que muy pocas mujeres consumen una segunda fruta diaria ó verduras más de una vez/día; sin embargo y con respecto al pescado y legumbres cabe destacar que el 70% declararon un consumo adecuado. En cuanto a la pasta y/o arroz y los frutos secos, como parte habitual de la dieta, se evidenció en porcentajes relativamente bajos, especialmente entre las estudiantes con sobrepeso.

En cuanto a los comportamientos con connotación negativa respecto a la DM señalar que entre las universitarias se encontraron porcentajes elevados que desayunan bollería industrial (55-62%) siendo mayoritario en aquellas con sobrepeso. En cuanto a los porcentajes de ingesta de dulces y golosinas varias veces al día (9-15%) es minoritario para el grupo de normopeso; mientras que, los comportamientos como acudir asiduamente a restaurantes de comida rápida (30,0%) son aproximadamente igual en los tres grupos.

Diferencias entre los grupos ponderales de Adhesión a la Dieta Mediterránea

En la tabla IV, se exponen y comparan los porcentajes del test Kidmed entre los tres grupos ponderales de adherencia a la DM (alta, media y baja) existiendo diferencias estadísticamente significativas ($p < 0,05$) entre cada uno de los grupos en los tres primeros ítems (es decir los ítems que más discriminan son los referidos específicamente al consumo de frutas y verduras).

Existen diferencias significativas ($p < 0,05$) parciales al comparar el grado de adherencia alta frente al de media y baja en los ítems 4, 6, 14 y 15 (referidos a con-

sumo de una segunda verdura, utilización de centros de comida rápida, desayuno de bollería industrial y consumo diario de yogures y/o queso). Asimismo con respecto a la adherencia alta y media frente a la baja en los ítems 5, 9, 12, 13 y 16 (correspondientes a consumo de pescado, desayuno con cereales y lácteos, o no desayunar, o consumir golosinas diariamente) y si se compara la adherencia alta frente a la baja se dan diferencias en el ítem 10 (tomar frutos secos). No se han encontrado diferencias significativas entre los tres grupos ponderales en los ítems 7, 8 y 11 (es decir los ítems que menos discriminan son los correspondientes al consumo de legumbres, de pasta y el de utilización del aceite de oliva).

Actividad física y adhesión a la Dieta Mediterránea

En la tabla V, se exponen y comparan las puntuaciones y los porcentajes del test Kidmed entre aquellos que no realizan ni media hora de actividad física diaria ($n = 72$; 34%) frente a los que sí realizan algún tipo de actividad física diaria ($n = 140$; 66%). Existiendo diferencias estadísticamente significativas ($p < 0,05$) con respecto a una alta adherencia a la DM (8-12 puntos) y en el test Kidmed (%) principalmente en las cuestiones referidas al desayuno (ítems 9, 12 y 14 respectivamente).

Aquellos que no realizan ninguna actividad física, obtienen porcentajes mayores en no desayunar —19,4%—, en la ingesta de bollería industrial —72,2%— y además presentan menores porcentajes en la toma de un cereal o derivado en el desayuno —50,0%— (frente a los porcentajes del 5,7%, 48,6% y 70%, respectivamente que se obtienen en los citados

Tabla V
Test Kidmed (puntuaciones y distribución de %) en relación a la actividad física

	<i>Ninguna actividad física (n = 72)</i>	<i>Alguna actividad física (n = 140)</i>
Puntuación total Kidmed (media $\pm$ DE)	5,4 $\pm$ 2,0	6,2 $\pm$ 2,5
<i>Grado de Adhesión a la DM</i>		
Alta 8-12 ptos. (%)*	11,1%	31,4%
Media 4-7 ptos. (%)	72,2%	54,3%
Baja $\leq$ 3 ptos. (%)	16,7%	14,3%
<i>% de Respuestas Kidmed</i>		
1. Toma 1 fruta o un zumo natural todos los días	88,9%	77,1%
2. Toma una 2ª pieza de fruta todos los días	27,8%	45,7%
3. Toma verduras frescas o cocinadas 1 vez al día	69,4%	64,3%
4. Toma verduras frescas o cocinadas >1 una vez al día	16,7%	32,9%
5. Consume pescado (por lo menos 2-3 veces a la semana)	66,7%	72,9%
6. Acude $\geq$ 1 vez a la semana a un centro de comida rápida	25,0%	30,0%
7. Las legumbres las toma más de una vez a la semana	72,2%	68,6%
8. Toma pasta y/o arroz (5 días o más a la semana)	22,2%	22,9%
9. Desayuna un cereal o derivado todos los días (pan,...) *	50,0%	70,0%
10. Toma frutos secos (al menos 2-3 veces a la semana)	22,2%	22,9%
11. Se utiliza aceite de oliva en casa	100,0%	98,6%
12. No desayuna todos los días *	19,4%	5,7%
13. Desayuna un lácteo (yogurt, leche,...)	91,7%	88,6%
14. Desayuna bollería industrial, galletas o pastelitos *	72,2%	48,6%
15. Toma dos yogures y/o 40 g de queso cada día	36,1%	48,6%
16. Toma golosinas o refrescos azuc. Varias veces al día	11,1%	11,4%

*Prueba Chi cuadrado con corrección de Bonferroni. Diferencias significativas ($p < 0,05$).

ítems para los que sí realizan actividad física diaria). En resumen, favorecer un desayuno de calidad y realizar al menos media hora de AF diaria son claves asociadas a la presencia de una alta ADM en el alumnado estudiado.

Discusión

El test Kidmed se ha venido utilizando, por su sencillez de interpretación para los encuestados y para el encuestador, para valorar la ADM de distintas poblaciones españolas^{7,8-16} y de otros países de nuestro entorno¹⁷⁻²². Aquí de nuevo hemos puesto en evidencia dicha facilidad de manejo al ser utilizado para la valoración de los hábitos de un grupo de universitarias madrileñas estudiantes del Grado de Magisterio de edades entre 21 y 24 años. El grupo en cuestión representa la tipología mayoritaria del alumnado que realiza dicha formación con lo cual los datos obtenidos pueden ofrecer una visión más amplia sobre este tipo de estudiantes sobre los que estudios del tipo que aquí presentamos suelen ser escasos.

En nuestro caso, al igual que en otras investigaciones recientes realizados con otros estudiantes españoles universitarios^{9,36,37} los elevados porcentajes de participantes con dietas de adhesión media y baja a la DM ponen de manifiesto la necesidad de tratar de mejorar la aproximación de sus hábitos a los patrones mediterrá-

neos. Así estarían el 75,5% de nuestras estudiantes, y si acotamos los datos de otros estudios al sexo femenino, en esa circunstancia estarían el 70,3% de universitarias navarras⁹ o el 68,9% de las alumnas gallegas³⁶.

En el mismo sentido, el dato que hemos obtenido de valor medio del índice Kidmed fue escasamente de 5,9 puntos; puntuación algo más baja que la que se obtiene en el análisis de ADM de universitarias navarras⁹ (que fue de 6,3) o en el caso de las alumnas gallegas³⁶ (con una media de 6,2). Es decir en términos generales la ADM de las futuras Maestras se situaría en valores claramente inferiores con respecto a otras universitarias referenciadas.

Asimismo se han analizado los datos de IMC de la muestra siendo similares al de estudios referenciados con otras universitarias como las gallegas³⁶ y se han comparado con los grados de adhesión a la DM (baja, media y alta) y tampoco se evidenciaron diferencias significativas entre ambos grupos de índices como ocurre en el estudio de las alumnas gallegas³⁶, aunque sí se encuentran diferencias entre éstos en otras investigaciones como en el caso de universitarias navarras⁹.

En cuanto a la comparativa de los datos de los distintos ítems del test Kidmed evidenciarían que con respecto a la toma diaria de una y dos frutas, frutos secos y desayunar un lácteo, los porcentajes son parecidos a los referenciados para universitarias navarras⁹, gallegas³⁶ y madrileñas³⁷. Con respecto a la toma de una o dos raciones de verduras los porcentajes son más parecidos a las

universitarias navarras⁹ y gallegas³⁶, pero inferiores a las madrileñas³⁷. Con respecto al consumo de pescado los porcentajes son parecidos a las universitarias gallegas³⁶, siendo superiores a los reportados por navarras⁹ y madrileñas³⁷. En cuanto a acudir a un centro de comida rápida o desayunar un cereal o derivado se parecen a las universitarias madrileñas³⁷, pero son superiores e inferiores respectivamente, a navarras⁹ y gallegas³⁶. En cuanto a las legumbres, pasta y/o arroz, como a no desayunar y tomar golosinas los datos son parecidos a las universitarias navarras⁹, mostrándose porcentajes superiores en cuanto al consumo de legumbres, e inferior al resto de los expuestos anteriormente para gallegas³⁶ y madrileñas³⁷. Con respecto al aceite de oliva los porcentajes son parecidos a gallegas³⁶ y madrileñas³⁷, y muy superiores a las navarras⁹. En cuanto a la toma de dos yogures y/o 40 g de queso los porcentajes son iguales a la de navarras⁹ y madrileñas³⁷, pero inferiores a las gallegas³⁶. Por último no presentan ningún parecido los datos sobre desayunar bollería industrial donde los porcentajes son mucho más altos que en navarras⁹ y gallegas³⁶. Resumiendo los datos porcentuales por ítems del test Kidmed son más parecidos a los obtenidos para universitarias navarras⁹ en 11 de los 16 ítems, frente a 8 de 16 de las universitarias madrileñas³⁷ y frente a 7 de 16 de las universitarias gallegas³⁶.

Lo expuesto anteriormente implicaría en nuestro estudio que para pasar de una dieta con adherencia mediterránea baja, a media y de está a una alta, sería necesario mejorar el consumo de frutos secos y pasta y/o arroz (que sólo lo hacen en un 22,6% de los casos), así como la toma de una segunda verdura ó pieza de fruta (realizado por el 26,4% y 38,7% respectivamente). Igualmente deberían reducirse el consumo de bollería industrial (el 56,6% la consume habitualmente), acudir menos asiduamente a un centro de comida rápida (que lo hacen un 29,3%) o tomar golosinas o refrescos azucarados (efectuado diariamente por el 11,3%) y no desayunar (que lo suprimen el 10,4%). Además hemos puesto en evidencia que entre las alumnas con IMC sobrepeso escasea el consumo de la pasta y/o el arroz y tienen porcentajes elevados en desayunos con bollería industrial.

No se evidenciaron diferencias significativas en cuanto a la puntuación total del cuestionario Kidmed y la realización o no de alguna actividad física (AF) diaria, aspecto que sí ponen en evidencia estudios realizados con adolescentes andaluces³⁰. Sí se constatan diferencias significativas en cuanto a la realización o no de actividad física respecto al grado alto de adhesión a la DM a favor de los ítems relacionados con el desayuno. Esto último implicaría que aquellas alumnas que realizan al menos media hora de actividad física diaria presentan mayor probabilidad de realizar un desayuno más saludable, consumiendo más cereales y derivados y, menos bollería industrial y claramente tienen mejor puntuación de ADM. Con lo cual serían también hábitos a considerar mejorar entre el resto del alumnado.

En cuanto a las limitaciones del estudio ofrecido aquí una de ellas sería el haber analizado exclusivamente estudiantes de sexo femenino (por otra parte mayoritario en la carrera de Magisterio). No obstante, a la luz de otros estudios que han analizado la ADM con universitarios^{9,36,37} no se suelen encontrar diferencias significativas a nivel de datos globales entre sexos. Por otra parte, otras cuestiones como el tipo de residencia de los estudiantes universitarios⁹ (familiar o independiente) podría haberse considerado u otras cuestiones de tipo sociológico que podrían condicionar en algunos casos la ADM³⁰.

A pesar de ello, la oportunidad e interés de ofrecer un estudio que profundice sobre la ADM que tienen futuros universitarios que van a ser formadores de niños o niñas parece evidente por su interés estratégico para así poder ofrecer alternativas de mejora. Máxime cuando se ha puesto en evidencia la necesidad de ésta en distintos hábitos considerados esenciales en la ADM, conductas que luego pueden transmitir en su labor profesional. Así, en conclusión, se ha puesto en evidencia la necesidad de establecer programas de mejora dentro de la formación de este alumnado universitario, en concreto en hábitos nutricionales como un desayuno más saludable (con menos bollería industrial), un consumo adecuado de frutas y verduras, incrementar los consumos de legumbres y pasta, etc.; u otros hábitos como el realizar un mínimo de ejercicio físico diario. Consideramos pues que las conductas relativas al patrón de dieta de tipo mediterránea deben favorecerse y mejorarse con programas apropiados en sus currículos formativos especialmente entre este tipo de futuro profesorado por la trascendencia social que ello puede tener.

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Original / Nutrición parenteral

Impact of parenteral nutrition standardization on costs and quality in adult patients

David Berlanda¹, Anna Barraquer¹, Pilar Sabin¹, Luisa Chicharro², Agueda Pérez³, Carolina Puiggrós², Rosa Burgos² and Julio Martínez-Cutillas¹

¹Servicio de Farmacia. Hospital Vall Hebron. Barcelona. España. ²Unidad de Soporte Nutricional. Hospital Vall Hebron. Barcelona. España. ³Servicio de Medicina Intensiva. Hospital Vall Hebron. Barcelona. España.

Abstract

Background: Parenteral nutrition (PN) is a costly therapy that can also be associated with serious complications. Therefore, efforts are focusing on reducing rate of complications, and costs related to PN.

Objective: The aim was to analyze the effect of the implementation of PN standardization on costs and quality criteria. Secondary aim was to assess the use of individualized PN based on patient's clinical condition.

Methods: We compare the use of PN before and after the implementation of PN standardization. Demographic, clinical and PN characteristics were collected. Costs analysis was performed to study the costs associated to the two different periods. Quality criteria included were: 1) PN administration; 2) nutrition assessment (energy intake between 20-35 kcal/kg/day; protein contribution according to nitrogen balance); 3) safety and complications (hyperglycemia, hypertriglyceridemia, hepatic complications, catheter-related infection); 4) global efficacy (as serum albumin increase). Chi-square test was used to compare percentages; logistic regression analysis was performed to evaluate the use of customized PN.

Results: 296 patients were included with a total of 3,167 PN compounded. During the first period standardized PN use was 47.5% vs 85.7% within the second period ($p < 0.05$). No differences were found in the quality criteria tested. Use of individualized PN was related to critical care patients, hypertriglyceridemia, renal damage, and long-term PN. Mean costs of the PN decreased a 19.5%. Annual costs savings would be € 86,700.

Conclusions: The use of customized or standard PN has shown to be efficient and flexible to specific demands; however customized PN was significantly more expensive.

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Key words: Parenteral nutrition. Parenteral nutrition quality. Parenteral methods. Parenteral nutrition economics.

Correspondence: David Berlanda.

Servicio de Farmacia.
Hospital Vall Hebron.
Pg Vall Hebron, 119.
08035 Barcelona. España.
E-mail: dberlanda@vhebron.net

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IMPACTO DE LA ESTANDARIZACIÓN DE LA NUTRICIÓN PARENTERAL EN COSTES Y CALIDAD EN PACIENTES ADULTOS

Resumen

Introducción: La nutrición parenteral (NP) es una terapia costosa asociada a serias complicaciones. De manera que muchos de los esfuerzos se centran en reducir estas complicaciones, así como los costes asociados.

Objetivos: Analizar el efecto de la estandarización de la NP en los costes y en indicadores de calidad. El objetivo secundario es estudiar la utilización de NP individualizada en función de las condiciones clínicas de los pacientes.

Métodos: Se compara la utilización de NP antes y después de la estandarización de la NP. Se recogen los datos demográficos, clínicos y características de la NP. Se realiza un análisis de costes asociados a los dos periodos de estudio. Se incluyen los siguientes indicadores de calidad: 1) Administración de NP; 2) Valoración nutricional (aporte calórico 20-35 kcal/kg/día; aporte proteico en función del balance nitrogenado); 3) seguridad y complicaciones (hiperglicemia, hipertrigliceridemia, complicaciones hepáticas, infección de catéter); eficacia global (aumento albúmina sérica). Se utiliza test de chi-cuadrado para comparación de porcentajes, y regresión logística para evaluar la utilización de NP individualizada.

Resultados: Se incluyeron 296 pacientes para un total de 3,167 NP. Durante el primer período el uso de NP estandarizada fue del 47,5% frente 85,7% en el segundo ($p < 0,05$). No se encontraron diferencias en los indicadores de calidad estudiados. La utilización de NP individualizada fue relacionada con pacientes críticos, hipertrigliceridemia y NP de larga duración. El coste medio de NP disminuyó en un 19,5%; pudiendo resultar un ahorro anual de 86,700€.

Conclusiones: La utilización de NP individualizadas o estándar ha mostrado ser eficiente y flexible; aunque el coste de la individualizada fue significativamente mayor.

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Palabras clave: Nutrición parenteral. Nutrición parenteral calidad. Nutrición parenteral métodos. Nutrición parenteral economía.

Abbreviations

PN: Parenteral nutrition.
MCB: Multichamber bags.
IPN: Individualized period.
SPN: Standardized period.
GGT: Gamma-glutamyl-transferase.
ALT: Alanine aminotransferase.
AST: Aspartate aminotransferase.
CRI: Catheter-related infection.
SD: Standard deviation.
OR: Odds ratio.

Introduction

Parenteral nutrition (PN) is an important supportive therapy indicated for patients whenever oral or enteral nutrition is not possible, insufficient or contraindicated. However, PN is a costly technology and can also be associated with complications such as electrolyte disturbances, hyperglycaemia, hypertriglyceridaemia, as well as hepatobiliary, infectious and mechanical complications.^{1,2}

Considerable research has focused on reducing complications and preventing errors associated with the administration of PN formulations. These complications can be minimized by careful patient selection, appropriate formulation, and close monitoring of the patient. Several guidelines have been developed to help clinicians with these complications of PN therapy.³ Therefore, an optimal implementation of PN plays an important role in reducing the risk of complications and optimizing the clinical outcome and the cost-efficiency ratio.

In times of budget constraints, attention is focused on cost-effectiveness treatments. In this way, since advantages in efficiency, economy, and clinical appropriateness with the use of standardized PN formulations compared with individualized PN formulations are suggested, a standardized process for PN management was developed in our hospital. The aim of this process was to reduce costs, reduce variation in PN formulations and promote uniformity among clinicians. The implementation of standardization of PN should have an optimal cost-efficiency ratio, seeking to reduce costs, reduce the risk of complications and opti-

mize clinical outcomes.

The aim of this study was to assess the economic and quality implications that might result from the implementation of PN standardization and greater use of standard PN in adult patients. The secondary aim was to report and assess the use of individualized PN based on the patient's clinical condition.

Methods

In June 2010, a standard PN regime in adult patients was introduced in our hospital for routine use. Following implementation of this new procedure the effects were assessed by retrospective analysis. Costs and type of PN formulations, and quality criteria on PN episodes in adult patients between February 2010 and May 2010 (IPN period) were compared with a similar group of patients who had received PN formulations between September 2010 and December 2010 (SPN period).

The Pharmacy Service, in agreement with the Nutrition Support Unit, developed a protocol for PN standardization, in compliance with accepted standards in the literature. Work was initiated in the Pharmacy Service to make standard PN solutions prepared in the pharmacy, based mainly on commercial multichamber bags (MCB). The compositions of these standardized solutions were chosen after considering normal requirements of adult patients with reference to the published literature and our own experience of PN. Standard commercial MCB used are listed in table I. The PN formulations were either prescribed individually or as standard solutions each morning based on the individual patient's clinical conditions and nutritional needs. The research protocol was authorized by the Ethics Committee of the Hospital.

Modification of standard PN solutions (by the addition of electrolytes and micronutrients to standard PN solutions) and preparation of individual PN solutions were performed by the pharmacy staff under laminar air flow units. However, most of the individualized PN solutions were prepared by subcontractor. We evaluated the frequency of standard solution prescriptions as MCB, and compared the utilization with standard vs. individual PN solutions in the following clinical conditions: renal impairment (defined as estimated glomerular

Table I
Standard MCB composition

	<i>Nitrogen (g)</i>	<i>Glucose (g)</i>	<i>Lipid (g)</i>	<i>Volume (mL)</i>
Oliclinomel® N7	6.6	160	40	1000
Oliclinomel® N4	7.3	160	40	2000
Nutriflex Lipid Special®	10	186	50	1250
Smofkabiven®	12	187	56	1500
Clinimix®	12	200	0	2000
Oliclinomel® N8	16.5	250	60	2000

filtration rate < 60 mL/min calculated by MDRD-4), long-term PN therapy (defined as patients who received at least 21 days of PN), hepatic impairment (defined as alkaline phosphatase > 280 IU/L, GGT > 50 IU/L or bilirubin > 1.2 mg/dL plus AST > 40 IU/dL or ALT > 42 IU/dL),⁴ critical illness (defined as inpatients in critical care units, included the intensive care post-recovery units), and hypertriglyceridemia (defined as serum triglyceride value > 400 mg/dL). Univariate logistic regression analyses were performed to estimate the association between the use of individualized PN and the variables such as the study period, and patient's clinical condition (renal impairment, long-term, hepatic impairment and critical illness).

The percentage of compliance in each quality criteria was compared to assess the quality implications resulting from the change of practice. Many factors might influence the quality of the PN therapy (e.g., compounding and administration of the solution, amounts of macro and micronutrients, nutrition assessment). To prevent under or overestimation of the effect of standardization in PN quality, only the quality criteria clearly related to this change of practice were assessed. These included 10 quality criteria that examined the following different areas: 1) PN administration; 2) nutrition assessment, adequacy of the nutrition support, and monitoring; 3) safety and complications; and 4) global efficacy of the PN regimen.⁵⁻⁷

- 1) PN administration:
 - a) Percentage of PN bags not administered and returned to Pharmacy Service.
- 2) Nutrition assessment, adequacy of the nutrition support, and monitoring:
 - a) Percentage of PN days with energy intake between 20-35 kcal/kg. Exceptions were peripheral PN and situations of hypertriglyceridemia (> 400 mg/dL).
 - b) Protein intake based on nitrogen balance. Percentage of PN days with insufficient protein intake. Protein intake is considered to be insufficient if nitrogenous balance is ≤ -2 if input is < 1.1 g protein/kg (except for patients in intensive care and post-recovery units, as their hypercatabolic state might be in an acute phase) Exceptions were patients with renal failure and peripheral PN.^{3,6,8}

The weight used for calculations was the actual body weight for all patients, except in obese subjects (body mass index > 30 kg/m²) where the ideal body weight was used.

- 3) Safety and complications.
 - a) Percentage of days with hyperglycemia, defined as glucose concentrations > 180 mg/dL.
 - b) Percentage of patients with hepatic complications; defined as the presence of 2 or more of

the following serum values: alanine aminotransferase (ALT) > 60 IU/L, aspartate aminotransferase (AST) > 60 IU/L, alkaline phosphatase > 220 IU/L, gamma-glutamyltransferase (GGT) > 80 IU/L, and/or bilirubin > 2 mg/dL after at least 10 days of PN. Hepatic complications rate was assessed separately as follows:

- i) Patients were excluded if any baseline liver function test was above the maximum reference value.
- ii) Patients were excluded if baseline values met our definition of liver impairment.
- c) Percentage of patients with hypertriglyceridemia, defined as triglyceridemia > 400 mg/dL. Patients with baseline serum triglyceride value > 250 mg/dL were excluded.
- d) Percentage of patients with at least a suspected catheter-related infection (CRI) that met diagnostic criteria. CRI was defined as the clinical signs of infection (fever, chills) in a patient with one or more positive blood culture obtained from a peripheral vein, and no apparent source of bloodstream infection except the catheter. In addition, the semi quantitative culture of the removed catheter was positive for the same microorganism isolated from the blood.⁹
- 4) Global efficacy of the PN regimen.
 - a) Percentage of patients who maintained or improved their nutrition status after PN. Defined as serum albumin level maintained or increased after at least 7 days of PN.
 - b) Percentage of patients who improved their nutrition status after PN. Defined as serum albumin level increased at least 0.2 g/dL from baseline after at least 7 days of PN.

A cost accounting model was used to perform a cost minimization analysis of the implications of transitioning to MCB use.¹⁰ The costs per PN included: cost of personnel, nutrition solutions, additives and medical supplies needed. The cost accounting model, manpower PN bag compounding time, and costs for all the processes involved in PN provision were based on our own data previously obtained. Price of the hospital-compounded bags used was the mean value obtained in the previous study. Meanwhile, the price of the individual PN bags performed by subcontractor was calculated using the combination of the average of the subcontractor selling price plus the costs of personnel, following the cost accounting model used. In the same way, for MCB, the costs of the nutrition solutions used were average manufacture's selling prices to our hospital for each commercial admixture used adding the costs of personnel obtained previously. Therefore, nutrient solutions and total cost date were recalculated.

We used a cost minimization model assuming the fact (under the hypothesis) of no change in quality in

Table II
PN and patients characteristics

	<i>IPN period</i>	<i>SPN period</i>	<i>Total</i>
<i>PN bags</i>	1769	1398	3167
MCB	840 (47.5%)	1198 (85.7%)*	2038 (64.4%)
Hospital & subcontractor-compounded	929 (52.5%)	200 (14.3%)	1129 (35.6%)
<i>PN characteristics</i>			
Peripherally/ Central PN	189/1580	181/1217	370/2797
Nitrogen (g)	11.9 ± 3.1	11.1 ± 3.0*	11.5 ± 3.1
Glucose (g)	200.5 ± 27.8	192.7 ± 27.9*	197.1 ± 28.1
Lipid (g)	43.8 ± 14.0	47.1 ± 15.5*	45.3 ± 14.8
Volume (mL)	1812.7 ± 266.0	1625.7 ± 338.5*	1730.1 ± 314.2
Total Kcal	1536.4 ± 276.3	1520.2 ± 283.2	1529.3 ± 279.4
<i>Patients</i>	145	151	296
Male (%)	64.8	54.3	59.5
Age (y)	62.8 ± 16.3	64.9 ± 15.3	63.9 ± 15.8
BMI (kg/m ²)	26.0 ± 12.1	25.3 ± 5.3	25.6 ± 9.2
PN days	14.1 ± 12.1	11.7 ± 14.3	12.9 ± 13.3
PN indication (%)			
Postoperative ileus & complications	37.2	43.0	40.2
Bowel rest	14.5	18.5	16.6
Obstruction	12.4	9.3	10.8
Malabsorption	6.2	10.6	8.4
Pancreatitis	6.2	4.6	5.4
Mucositis	4.8	4.0	4.4
Fistula	4.1	1.3	2.7
Others	14.5	8.6	11.5
ICU admission (%)	49.0	48.3	48.6
Death (%)	20.0	12.6	16.2

Values are expressed as mean ± SD, or %.

*p < 0.05.

the PN therapy, and therefore the lack of clear clinical differences between the two periods studied. We ran the cost model under two scenarios studied depending on the percentage of individualized PN obtained.

The patients were identified from the pharmacy records of all patients to whom PN was dispensed. Anthropometric and clinical parameters, as well as indication, duration and amounts of PN, were collected from the pharmacy, medical and nursing records. Results were expressed as number and percentage, mean ± standard deviation (SD). The data were analyzed by T-test for continuous variables in both groups and by Mann Whitney test in the event of an abnormal distribution. Quality variables were analyzed using a Chi-square test. All statistical analyses were performed with Stata software, release 11.0 (Stata Corporation, College Station, Texas); and statistical significance is reported for p < 0.05.

Results

During the two periods studied, a total of 3167 PN solutions were made for 296 adult patients; 145 in the IPN period before standardization implementation and 151 in the SPN period after the implementation. Three patients previously on home PN treatment were excluded. Of the

total number of PN performed, 1129 (35.6%) were hospital or subcontractor compounded and 2038 (64.4%) were as standard commercial three-compartment bags. Overall, 85.7% of the PN used within the SPN were commercial MCB, significantly higher compared with 47.5% in the IPN period (table II).

Differences in amounts of nutrient and volume of the PN between the two periods were found although not energy intake (table II). No significant differences were seen between groups among demographic parameters. Nevertheless, higher percentage of male patients was found within the first period. Details of PN utilisation are shown in table II. More than a third of patients were started on PN for postoperative ileus or postoperative complications.

No significant differences were found between the percentage of compliance in the 10 quality criteria compared (table III). No difference was observed in the incidence of hepatic complication between the two periods studied. None of the patients met the criteria of hepatic complication when excluding patients with any baseline liver function test altered. A small decrease in the percentage of patients who met criteria of CRI was observed. However, this decrease was not statistically significant. The overall line sepsis rate was 4.4 and 1.8 per 1000 PN days within the IPN and SPN period, respectively.

Table III
Quality criteria results

	<i>IPN period</i>	<i>SPN period</i>
1. PN indication		
a) PN no administered	0.8	0.6
2. Adequacy of the PN & monitoring		
a) Energy intake 20-35 Kcal/kg	70.8	73.7
b) Insufficient protein intake as nitrogen balance	4.5	5.1
3. Safety & complications		
a) Days of hyperglycemia	19.5	20.5
b) b. ii. Hepatic complications	12.4	8.1
c) Hypertriglyceridemia	10.8	7.7
d) Catheter-related infection	6.2	2.0
4. Global efficacy		
a) Albumin maintain	44.0	44.7
b) Albumin improvement	30.0	31.6

Values are expressed as %.

Overall, clinical conditions associated with customized PN use (hospital compounded or by subcontractor) on univariate analysis were: renal impairment, long-term PN, critical illness, and hypertriglyceridemia. However, before the standardization was enacted, long-term PN was not related to customized PN use (Odds Ratio [OR]: 1.04 [CI: 0.86-1.25]). Pre-standardization period was significantly associated with utilisation of individualized PN (table IV).

The mean cost of individualized PN formulations produced by the pharmacy department or subcontractor was €63.1 ± 6.1 per bag, compared to €39.5 ± 6.1 per bag of MCB. Based on the utilisation of each formulation, the mean cost of PN bag administered for the first period was significantly higher than the mean cost during the SPN period (52.4 ± 13.2 vs. 42.2 ± 9.8, $p < 0.05$). Meanwhile, the cost for all PN formulations during the IPN period was estimated at €92,773.1, compared to €59,058.9 for the SPN period.

According to the cost accounting model used, the standardization of PN was associated with cost savings of €10.2 (19.5%) per patient per day compared with the

previous period. Therefore, a total saving of €18,054 would be obtained within the first period. Consequently, in a large facility such as our hospital, savings for a mean of 8,500 PN bags per year would be €86,700.

Discussion

In this study we analyzed the changes in PN support after implementation of standardization for the adult patients in our hospital. In support of the primary hypothesis, this study found that after standardization, using commercial MCB as standard PN, cost of PN dropped significantly without negative effects on PN care quality.

The standard solutions in this study were manufactured as MCB solutions. Five commercial MCB were chosen as standard solutions. The formula selection was made based on similarities to those most frequently employed and those previously used. Therefore, costs were calculated for each commercial MCB used. Costs used for calculation were based on our own

Table IV
Use of costumized PN regarding clinical condition and period studied

<i>Clinical condition</i>	<i>IPN period</i>		<i>SPN period</i>		<i>All</i>	
	<i>Customized</i>	<i>OR (CI 95%)</i>	<i>Customized</i>	<i>OR (CI 95%)</i>	<i>Customized</i>	<i>OR (CI 95%)</i>
Renal impairment	364 (73.7)	3.51 (2.79-4.42)*	74 (18.1)	1.51 (1.11-2.07)*	438 (48.5)	2.14 (1.83-2.51)*
Long-term PN	402 (53.0)	1.04 (0.86-1.25)	95 (19.5)	1.86 (1.38-2.52)*	497 (39.9)	1.35 (1.17-1.57)*
Hepatic impairment	338 (52.6)	0.99 (0.83-1.22)	68 (15.0)	1.09 (0.79-1.49)	406 (37.0)	1.10 (0.94-1.28)
Critical illness	507 (73.9)	4.43 (3.59-5.46)*	128 (23.8)	5.59 (4.00-7.80)*	635 (51.9)	3.16 (2.72-3.68)*
Hypertriglyceridemia	149 (68.7)	2.17 (1.60-2.93)*	83 (38.1)	3.43 (2.51-4.69)*	232 (53.3)	2.34 (1.90-2.87)*
Period	929 (52.5)	—	200 (14.3)	—	1130 (35.7)	6.63 (5.57-7.91)*

Values are expressed as number of customized PN (%).

OR: Odds ratio; CI: confidence Interval.

* $p < 0.05$.

Table V
Overall costs, per period and per PN bag, in Euros

	Pre-Standardization	Post-Standardization	Total
<i>MCB standard</i>	40.1 ± 6.7	39.1 ± 5.6	39.5 ± 6.1
Manpower	5.1	5.1	5.1
Material	35.0 ± 6.7	34.0 ± 5.6	34.4 ± 6.1
Estimated total cost	33667.5	48689.8	80537.3
<i>Hospital & subcontractor-compounded</i>	63.6 ± 5.4	60.9 ± 8.4	63.1 ± 6.1
Manpower	4.0 ± 1.4	4.6 ± 2.2	4.1 ± 1.6
Material	59.6 ± 6.7	56.3 ± 10.6	59.0 ± 7.7
Estimated total cost	59105.6	12189.1	66671.2
All PN bags	52.4 ± 13.2	42.2 ± 9.8*	47.9 ± 12.8
Estimated total cost	92773.1	59058.9	136814.7

Values are expressed as mean ± SD, or %.

*p < 0.05.

data previously obtained.¹⁰ Moreover, we added costs of customized PN prepared by an outsourced center. The mean difference of €10.2 per bag gives the possibility of a cost reduction near to 20% related to PN costs. Overall, there was an important decrease in cost of PN after standardization with a total saving of €86,700 per year.

Apart from the analysis of costs, we assessed the impact of standardization on PN care quality. In the evaluation of the intervention program, the indicator should be chosen to establish the effectiveness, efficiency, and efficacy rate of the program.¹¹ Ten criteria were selected to evaluate our work on standardization of PN. There are several quality criteria related to PN support;^{5-7,11} however, we assessed the quality criteria clearly related to the intervention described. Therefore, quality indicators assessed were related to PN administration; nutrition assessment, nutritional requirements, patient monitoring, safety, and outcomes evaluation of the PN regimen. Although indicators regarding PN administration might not be affected by the change of practice, we selected the percentage of PN bags not administered and returned to the Pharmacy Service, since standardization has a better use of PN bags. Standardization could lead to re-utilization of the PN bags returned. Thus, 1% of returned standard PN bags for a mean of 8,500 PN bags per year might obtain a savings of €3,587 per year. The economic impact of clinical interventions to optimize PN care should be considered to achieve quality improvement.¹¹

This quality control study shows that after standardization of PN formula no modification was found with regard to quality indicators assessed. Indeed, most of the indicators assessed showed a slight improvement. However, this might be due to an initial effect of the standardization training. Therefore, in order to avoid this effect, the second study period started 3 months after implementation of the standardization. The available evidence comparing commercial standardized with customized PN with regard to patient safety is

limited.^{12,13} According to our results, the use of commercial MCBs do not modify the PN quality care and therefore do not increase the risk of complications related to PN. Nevertheless, standard PN formulations have been related to metabolic complications⁷ although the definition of metabolic complications by the authors included electrolyte disturbances, hypo- and hyperglycemia, and not hepatic complications. Furthermore, some of the commercial standard MCBs used in our study were without electrolytes; thus, electrolytes would be added according to the compatibility of the admixture and the patient's clinical condition. In contrast, more recently Turpin et al. reported an association between the use of MCB and lower rate of CRI compared to the rate associated with the use of pharmacy-compounded PN.^{14,15} As infusate contamination is a rare cause of CRI, we believe that most of the CRI are related to errors and catheter care, rather than due to the type of PN formulation. In addition, the compounding of PN admixtures must be made under strict aseptic conditions. Therefore, more studies should explore this issue in the future. However, no differences were found related to CRI in our study.

The use of commercial MCB is widespread in Europe. According to surveys performed in Switzerland and Spain, most PN for hospitalized adults were administered as commercial MCB.^{16,17} Furthermore, it seems that compounding of customized PN solutions takes place in medium to large facilities. Most hospitals offer between one to four different PN formulas, and two- and three-compartment bags were used. In the past, the potential disadvantage to MCB appeared to be the limited range of formula available. However, there are currently a large variety of standard MCB solutions on the market. A two-compartment system has been used as standard PN; it means that the addition of lipids to the bag is needed in order to deliver a total PN. Besides, electrolytes and nutrients such as glutamine might be added to the standardized bag because these criteria have been considered in the development of the

formulation. In this way, standardization of PN has been developed to a new way called “modular”.¹⁸ That means that from adding different macro- or micronutrients to standard formulations, a customized PN can be obtained. In addition to cost savings, the use of standard solutions might lead to reduce calculation errors as well as the risk of microbiological contamination, since there is a reduction in the handling of the constituents of the PN solution.^{13,19,20}

We evaluated the current PN practice, which includes a variety of prescribing and compounding methods, including customized PN based on the patient’s clinical condition. The use of customized PN was related to the following clinical conditions: long-term, renal impairment, hypertriglyceridemia and critical illness; similar to previously reported.²¹ Our study showed that after the intervention, the use of standard PN was 85%. This finding is in keeping with the results of other authors who suggested that three standard PN formulations might cover the macronutrient needs of 82% of patients.²² It is suggested that patients for whom standardized PN might be difficult to use include those with renal, hepatic or other organ compromise, critical illness and home PN.¹³ Long-term PN patients are more likely to receive customized PN formulations in order to avoid metabolism associated with long-term PN therapy. Critical illness is typically associated with a catabolic stress state in which patients commonly demonstrate a systemic inflammatory response. This response is coupled with complications such as multi-organ dysfunction, leading to alterations in electrolyte balance as well as in macronutrient metabolism. Renal impairment affects water, electrolyte and acid-base metabolism; but also induces alterations in protein, carbohydrate and lipid metabolisms. In addition, renal impairment has been related to episodes of hypertriglyceridemia and hyperglycemia in patients receiving PN.^{23,24} Therefore, it appears that patients with renal impairment should receive customized PN. In contrast, European guidelines suggest that standard PN formulation should be used in chronic kidney disease patients when PN is indicated.²⁵ However, European guidelines on PN and surgery indicate that standardized nutritional support cannot be applied to patients with chronic renal failure.²⁶ Therefore, standard PN solutions should be assessed in each facility to know how they might be used.

In comparison to the first period, the glucose and protein content of PN admixtures were on average lower within the standardization period. But the mean lipid content was significantly higher during this second period. However, on percentage, the differences found in macronutrients were less than 8%. This represents a mean difference of 0.8 g of nitrogen, 7.8 g of glucose and 3.3 g of lipids. We assume that standard PN solutions might be used in an even larger proportion of patients than observed in our evaluation, since we did not detect an increase of complications. Besides, little differences in macronutrient amounts were found.

The authors acknowledge that this was a retrospective study; thus, the data limit us to identifying potential associations. However, our findings may contribute to an open discussion regarding the use of MCB and customized formulations. Current PN practice includes prescribe and compound PN methods, including customized PN formulations based on the patient’s clinical condition. In fact, the two periods compared included both those patients who received PN compounded in the hospital pharmacy or by an outsourced centralized compounding center and patients receiving commercial MCB. The decision regarding PN choice can be complex; it would be influenced by the number and type of patients requiring PN within a specific clinical situation.

In conclusion, the use of both kinds of PN, customized or commercial MCB, has shown to be efficient and flexible to the specific demands. However, greater use of customized PN was significantly more expensive. Our study has demonstrated that PN standardization can bring about cost-containment without compromising PN quality care.

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Original / *Nutrición parenteral*

Outcomes of a general hospital-based Home Parenteral Nutrition (HPN) program; report of our experience from a 26-year period

Isabel Higuera¹, Pilar Garcia-Peris¹, Miguel Cambor¹, Irene Bretón¹, Cristina Velasco¹, Rosa Romero², Laura Frias¹ and Cristina Cuerda¹

¹Unidad de Nutrición Clínica y Dietética. Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón. Madrid. España. ²Servicio de Farmacia. Hospital General Universitario Gregorio Marañón. Madrid. España.

Abstract

Background: Home parenteral nutrition (HPN) was introduced in Spain in the late 1980s. Our hospital was a pioneering medical centre in this field.

Aim: Analyze outcomes of our HPN program.

Methods: Retrospective study of patients receiving HPN between 1986-2012. Study variables are expressed as frequency, mean $\pm$ SD (range), median [interquartile range]. Parametrics, non-parametrics test and survival analysis ($p < 0.05$) were applied.

Results: 91 patients (55 females and 36 males, mean age: 50.6 ± 5 yrs.) who received HPN for an accrual period of 55,470 days (median: 211 days [range: 63-573]) were included. The most prevalent underlying condition was cancer (49.5%), with the commonest HPN indication being short bowel syndrome (41.1%). The most frequently used catheter type was the tunneled catheter (70.7%). The complication rate was 3.58/1,000 HPN days (2.68, infection; 0.07, occlusion; 0.07 thrombosis; and 0.59, metabolic complications). Complications were consistently associated with both the underlying condition and HPN length. Infections were most frequent within the first 1,000 days of HPN. Liver disease incidence was related to HPN duration. HPN could be discontinued in 42.3% of patients. Ten-year survival rate was 42%, and varied across the underlying conditions.

Conclusions: In the present series, the commonest reason for HPN was cancer. Our complication rate is in keeping with that reported in the literature. The overall survival rate was 42%, and varied across the underlying conditions.

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Key words: *Home parenteral nutrition. Complications. Survival.*

Correspondence: Isabel Higuera Pulgar.
Unidad de Nutrición Clínica y Dietética.
Hospital General Universitario Gregorio Marañón.
Instituto de Investigación Sanitaria Gregorio Marañón.
C/ Doctor Esquerdo, 46.
28007 Madrid. España.
E-mail: ihiguera86@gmail.com

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RESULTADOS DEL PROGRAMA DE NUTRICIÓN PARENTERAL DOMICILIARIA (NPD) DE UN HOSPITAL GENERAL; ANALISIS DE 26 AÑOS DE ACTIVIDAD

Resumen

Introducción: La nutrición parenteral domiciliaria (NPD) se introdujo en España a finales de 1980. Nuestro hospital fue pionero en este campo.

Objetivo: Analizar los resultados de nuestro programa de NPD.

Métodos: Estudio retrospectivo de los pacientes que recibieron NPD entre 1986-2012. Las variables se expresan como frecuencias, media $\pm$ DE (rango), mediana [intervalo intercuartílico]. Se aplicaron pruebas paramétricas, no paramétricas y análisis de la supervivencia ($p < 0,05$).

Resultados: 91 pacientes (55 mujeres, edad media: $50,6 \pm 5$ años). La duración total del tratamiento con NPD fue de 55.470 días (mediana: 211 días [rango: 63-573]). El diagnóstico principal y la indicación de NPD más frecuentes fueron el cáncer (49,5%) y el síndrome del intestino corto (41,1%). El tipo de catéter más utilizado fue el tunelizado (70,7%). La tasa de complicaciones totales fue de 3,58/1.000 días HPN (2,68 para infecciones; 0,07, oclusiones; 0,07 trombosis, y 0,59, complicaciones metabólicas) y se asoció al diagnóstico principal y la duración de la NPD. Las infecciones fueron más frecuentes en los primeros 1.000 días de NPD. La incidencia de hepatopatía se relacionó con la duración de este tratamiento. En el 42,3% de los pacientes se pudo suspender la NPD. La tasa de supervivencia global a los diez años fue del 42% con diferencias entre los diagnósticos principales.

Conclusiones: En nuestra serie, la razón más común para la NPD fue el cáncer. Nuestra tasa de complicaciones esta acorde con la literatura. La tasa de supervivencia global fue del 42%.

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Palabras clave: *Nutrición Parenteral Domiciliaria. Complicaciones y supervivencia.*

Abbreviation

HPN: Home Parenteral Nutrition.

ESPENHAN-CIF group: Home Artificial Nutrition and Chronic Intestinal Failure Group of the European Society for Clinical Nutrition and Metabolism.

NADYA-SENPE: Working Group on Home and Outpatient Artificial Nutrition of the Spanish Society for Parenteral and Enteral Nutrition.

SD: Standard deviation.

IQ: Interquartile range.

i.e.: “id est”, that is.

e.g.: “exempli gratia”, for example.

MCT: Medium Chain Triglycerides.

LCT: Long Chain Triglycerides.

PICC: Peripherally Inserted Central Catheter.

MBD: Metabolic Bone Disease.

Introduction

Home parenteral nutrition (HPN) gives rise to long-term survival of patients with permanent or transient intestinal failure.¹ More than 45 years have passed since this modality of nutritional support was first used in 1967.² In most countries, HPN is most often hospital-based and is generally delivered by specialized multidisciplinary teams.³

According to data from the 2011 survey by the Home Artificial Nutrition and Chronic Intestinal Failure Group of the European Society for Clinical Nutrition and Metabolism (ESPENHAN-CIF group),⁴ HPN prevalence lies within the range of 3.25-66 patients/million. In Spain, HPN prevalence, as estimated based on data from the voluntary register of the Working Group on Home and Outpatient Artificial Nutrition of the Spanish Society for Parenteral and Enteral Nutrition (NADYA-SENPE), has been increasing since the register was first opened, with the prevalence rate being of 4.06 patients/million in 2012,⁵ and an unequal distribution throughout the country.⁶

The major HPN complications are those associated with the venous catheter (i.e. infection, occlusion and venous thrombosis) and those of metabolic nature (i.e. liver disease and metabolic bone disease).⁷

In order to share our group's experience, herein we report the outcomes of a general hospital-based HPN program covering a 26-year period; that is, since the program was first implemented in our hospital.

Aim

Analyze outcomes of our HPN program.

Methods and materials

A longitudinal retrospective study including all patients treated at the Hospital General Universitario

Gregorio Marañón (Madrid, Spain) who received HPN between January 1986 and October 2012 was conducted. Study data were collected from both medical records and the HPN register of the NADYA-SENPE group (www.nadya-senpe.com). Data collection was compliant with the Law on Protection of Personal Data (Spanish Organic Law 15/1999). More than one HPN episode for each patient was allowed. A new HPN episode was identified when HPN administration was suspended for longer than 3 months regardless of the reason (e.g. protracted hospital stay, attempt to HPN discontinuation).

Data statistical analysis was conducted by patient for the following variables: age at HPN initiation, underlying condition (diagnosis), number of catheters, clinical evolution and survival. Data analysis was carried out by HPN episode for the following variables: HPN indication, type of catheter, patient activity and independence levels and number and type of HPN-associated complications.

The diagnosis of catheter-related infectious complications was performed in accordance with the definitions by the Center for Disease Control.⁸ Catheter occlusion was defined as either impossibility of infusing any fluid or drawing blood through the catheter or need of exerting an excessive pressure or both. The diagnosis of central venous thrombosis was made based on clinical data (i.e. thorax, shoulder or neck pain with signs suggestive of venous occlusion with ipsilateral arm edema or superior vena cava syndrome) and confirmation by upper limb venography or Doppler sonography.⁹ The diagnosis of HPN-associated liver disease was established based on an 1.5-fold elevation of the upper limit of normal persisting for at least 6 months in serum levels of two of the following parameters: -glutaryl transferase, alkaline phosphatase and/or conjugated bilirubin.¹⁰ In some instances, liver disease diagnosis was made by liver biopsy. Metabolic bone disease (MBD) was defined as skeletal fragility due to abnormal bone quality either in asymptomatic patients or in patients presenting with bone pain and/or fracture.¹¹ MBD was diagnosed by adhering to the WHO criteria, which define osteopenia as a T-score between -1 and -2.5 standard deviations (SD) and osteoporosis as a T-score below -2.5 SD.

To address the impact of the changes implemented in our clinical practice over the 26-year period covered by the study, we took into account that: (1) initially, HPN solutions were elaborated at the Hospital pharmacy, and since 1998 the hospital reached an agreement with a pharmaceutical company, which delivered HPN solutions at patients' home; (2) In January 2007, we started using lipid formulations composed of mixtures of medium chain triglycerides (MCT), long chain triglycerides and 3, rather than 50% MCT/LCT mixtures; and (3) since 2009, tunneled catheters in use have been sealed with saline solution instead of sodium heparin, with the sealing being maintained with heparin in subcutaneous reservoir catheters.

To address the relationship of variable underlying condition (i. e. diagnosis) to survival, all types of malignancy on either active or palliative therapy were unified together in the variable *malignant neoplasms*, while under the variable *other underlying conditions* motility abnormalities and congenital disorders were brought together since no patients on HPN died from a condition included in the latter variable.

For data statistical analysis, the absolute and relative (percentage) frequency, mean, standard deviation (SD), median, range, and interquartile (IQ) indexes were used. Sample normality was tested by means of Kolmogorov-Smirnov test for independent samples. T-Student,² Kruskal-Wallis and Mann-Whitney tests, ANOVA and bivariate correlations were used as well. Survival was analyzed by Kaplan-Meier method and the log rank test. To determine the impact of HNP-related factors on survival, both univariate and multivariate analyses were conducted. The variables gender, age, diagnosis and catheter-related infectious and liver complications were included in the univariate analysis, whereas Cox regression model was used to estimate predictive values for death. Then, factors showing statistical significance were included in the multivariate analysis. Statistical significance was set at $p < 0.05$. All statistical tests were conducted by means of the software package IBM SPSS® Statistics 21.

Results

Patients' characteristics

A total of 91 patients (36 males and 55 females) were included in the study. There were 116 HNP episodes (mean and SD: 1.27 ± 0.67 per patient; range: 1-5 episodes). The distribution by number of HPN episodes was: 80% of patients with 1 episode, 15.4% with 2 episodes, 2.2% with 3 episodes and only 1.1% achieved 4 and 5 episodes. Mean age at HPN initiation was 50.6 ± 15 years (range: 3 months-83 years). The most frequent diagnosis was the neoplasms on palliative therapy in the 34.1%, followed by neoplasms on active therapy and radiation enteritis (15.4%), mesenteric ischaemia (12.1%), Crohn disease (5.5%), motility abnormalities (2.2%), congenital anomalies (1.1%) and other diagnoses (14.3%). The total duration of HPN was 55 470 days (median per patient: 211 days [IQ: 63-573]; median per HPN episode: 184 days [IQ: 59-531]). Significant differences in mean HPN duration across the underlying conditions were found ($p = 0.007$). The most common indication for HPN was short bowel syndrome (41.1%) (fig. 1). Patients' activity level was normal in 18.8% of cases and limited in 71.8%, with 8.5% of patients being bedridden or confined to the armchair. Patients' independence level was complete in 49.6% of cases and limited in 48.7%. Both activity and independence levels were correlated with the underlying condition ($p < 0.001$).

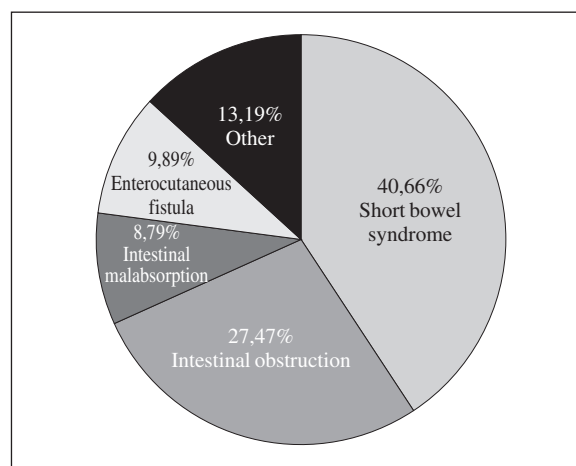


Fig. 1.—Distribution of patients by HPN indication.

HPN characteristics and complications

A total of 146 catheters were used (mean: 1.8 ± 1.5 per patient; range: 1-9). The most frequently used venous catheter was the tunneled catheter (70.7% of patients), followed by the reservoir catheter (28.4%). In our series, only one peripherally inserted central catheter (PICC) was used. The type of catheter was correlated with the underlying condition ($p = 0.001$).

The total number of complications was 199 (mean complication rate/1,000 HPN days: 3.58). Catheter-related infectious complication rate was 2.68/1,000 HPN days, while catheter-related non-infectious complication rate was 0.31 (0.07/1,000 HPN days for occlusion, 0.07/1,000 HPN days for venous thrombosis, and 0.17/1,000 HPN days for other complications, such as catheter wear or rupture). Infectious complication incidence was highest within the first 1,000 HPN days (fig. 2) ($p < 0.001$) (RHO = 0.47). Also, a correlation between infectious and thrombotic complications was found ($p < 0.001$).

Metabolic complications were seen in 28.6% of cases. Eight patients (8.8%) developed liver complications with varying clinical evolution: 4 had mild liver disease without cholestasis, and 2 of them died from their underlying condition; 4 patients had severe liver disease with attendant cholestasis (2 of them died due to HPN-associated liver failure, 1 experienced clinical improvement when lipids were removed from the HPN solution, and 1 child is pending hepatointestinal transplantation). Median HPN duration before the development of liver disease was 279 days (IQ: 165-1013). Liver complications were correlated with HPN duration ($p < 0.05$).

In 17 patients who had a bone density test done while on HPN, the mean lumbar T-score was -2.37 ± 1.4 , while mean femoral neck T-score was -2.41 ± 1.03 (table I). Furthermore, MBD was correlated with the underlying condition ($p = 0.012$) and patients' independence level ($p = 0.02$). Differences in MBD

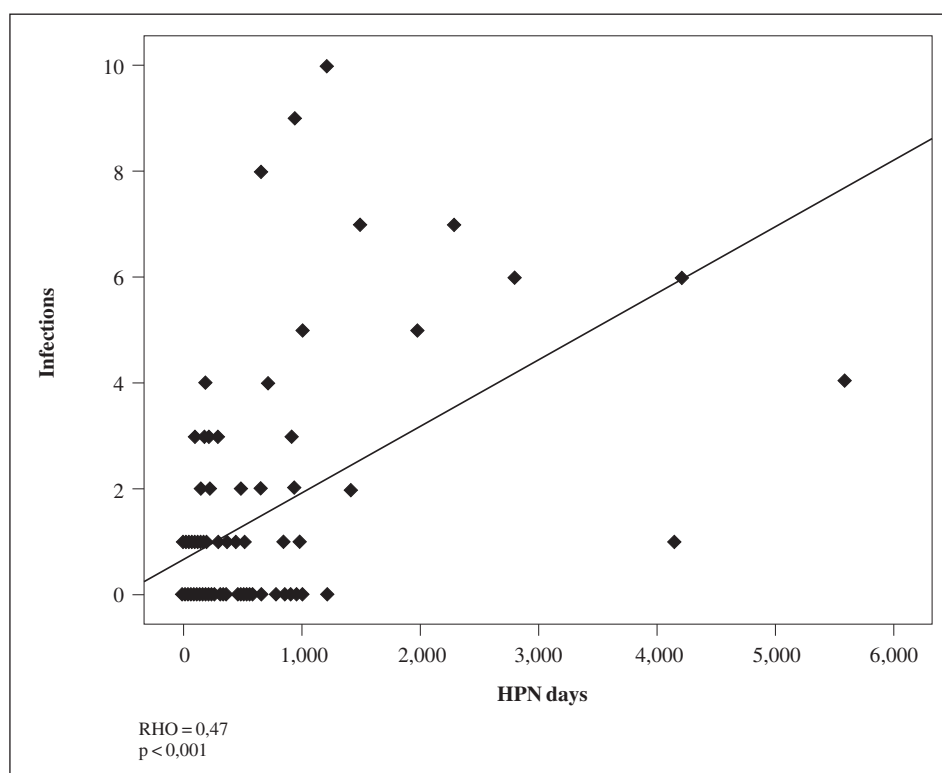


Fig. 2.—Infectious complications by HPN duration.

Table I
Distribution of metabolic bone disease in HPN patients

	<i>Bone densitometry during HPN</i>	
	<i>Lumbar spine % (patients)</i>	<i>Femoral neck % (patients)</i>
Normal	26,3 (5)	15,8 (3)
Osteopenia	26,3 (5)	36,8 (7)
Osteoporosis	47 (9)	47,4 (9)

between males and females at lumbar ($p = 0.04$) and femoral ($p = 0.02$) levels were found.

Overall complications were correlated with both the underlying condition ($p = 0.001$) and HPN duration, with a 6-fold increment in the risk of complication development for patients on HPN for more than 180 days as compared with those on HPN for less than two months ($p = 0.001$).

When the first 13 years were compared with last 13 years of our HPN experience, we encountered a significant increase in the use of HPN for cancer (45.1% increment), Crohn disease (5.5%) and radiation enteritis (6.6%) ($p = 0.004$), whereas the HPN use for mesenteric ischaemia or motility abnormalities remained stable. Additionally, overall mean complication ($p = 0.01$) and catheter-related complication rates, both infectious and non-infectious ($p < 0.001$), declined during the last 13 years. We found no significant differences in the emergence of tunneled catheter-related complications following the switch from heparin to saline for catheter

sealing. Since the introduction of the lipids - MCT/LCT/ 3 mixtures, the catheter-related non-infectious complication rate has dropped (from 1.1/1,000 HPN days to 0.8/1,000 HPN days, $p < 0.05$).

Clinical evolution and survival analysis

Based on clinical evolution outcomes, 30 patients (42.3%) were weaned off HPN following intestinal adaptation; 3 (4.2%) developed end-stage chronic renal failure and were switched to intradialytic parenteral nutrition; 11 (15.5%) discontinued treatment due to other reasons; and 27 (38%) died. At present, 20 patients remain on HPN. Overall survival rate at 1, 3 and 5 years after HPN initiation was 72%, 58% and 42%, respectively. In the case of patients suffering from a non-malignant condition, 10-year survival rate was 65%. We found statistically significant differences in survival across the underlying conditions (fig. 3). The univariate analysis results showed that the underlying condition and catheter-related infectious complications significantly influence mortality (table II). In the multivariate analysis, only the variable underlying condition showed to independently influence survival ($p < 0.05$).

Discussion

Currently, HPN is widely recognized as a safe, efficient therapy whose development has paralleled both parenteral

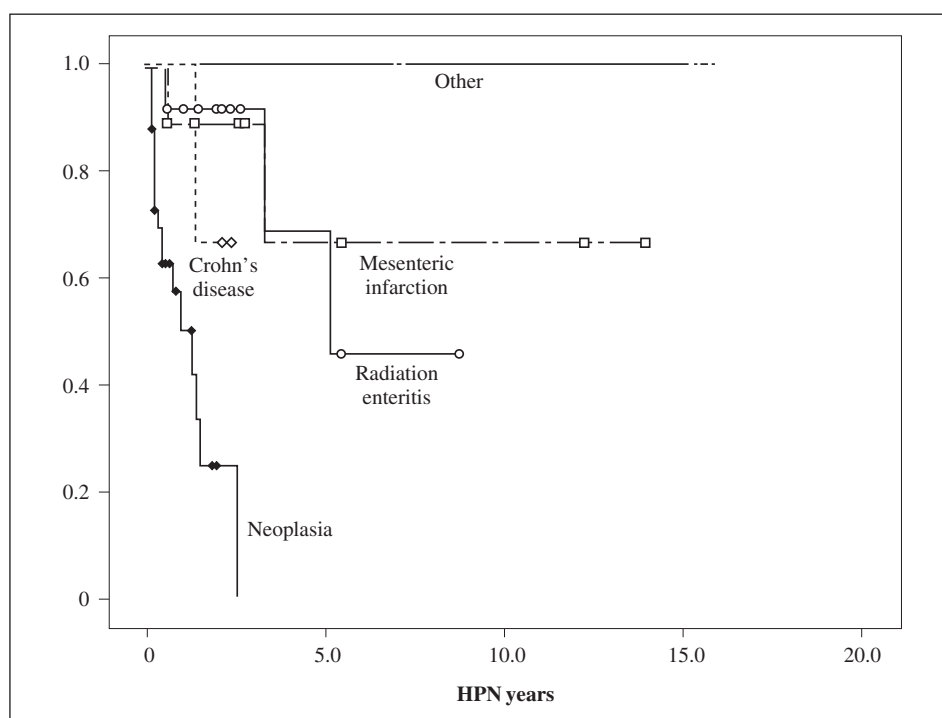


Fig. 3.—Survival by underlying condition.

Table II
Effect of the addressed variables on survival

Variable	Group/rank	Hazard ratio (95% CI)	P-value
Diagnosis	Neoplasias	1	
	Radiation enteritis	0,72 (0,01-0,37)	0,002
	Crohn's disease	0,23 (0,03-1,72)	0,15
	Mesenteric infarction	0,52 (0,008-0,35)	0,002
	Others	No event	
Catheter-related infectious complications	Lineal	0,27 (0,11-0,64)	0,003
	No	1	
	1	0,34 (0,11-1,03)	0,057
	> 1	0,23 (0,08-0,65)	0,005

nutrition evolution itself (e. g. catheters, formulas) and healthcare providers' improved knowledge and practical experience.¹² In the present paper, we look back over our HPN experience with a large patient cohort that has been investigated by means of a long-term follow-up.

In our series, the most frequent HPN indication was short bowel syndrome, which concurs with findings reported from other series in Spain, Europe and the United States.¹³ In some countries, malignancy has now replaced benign conditions as the most usual etiology of intestinal failure leading to HPN.^{12,14} However, the use of HPN in patients with terminal cancer has obvious cultural and religious implications, and widely varies from one country to another. Indeed, in certain European countries, benign conditions, such as Crohn disease, intestinal ischaemia and intestinal pseudoobstruction, continue to be the most commonly diagnosed underlying conditions in HPN patients.¹⁵

In the present series, the most frequently used catheter type was the tunneled catheter, followed by the reservoir and PICC catheters, which coincides with the standards in Spain.^{5,16} The tunneled catheter is of first choice for patients with underlying benign condition, whilst the reservoir catheter is still the most widely used in cancer patients, probably because this type of catheter allows access compatibility for intravenous chemotherapy; however, this is not the case in all the countries reported in the literature.¹⁴

Catheter-related infectious complications were the most common in our patients, with a rate of 2.68/1,000 HPN days, which is slightly higher than the average incidence of 1-2 episodes/1,000 catheter days reported in earlier series,¹⁷ but lies still within the standard range (i.e. 0.38-4.58 episodes/1,000 catheter days).¹⁸ Catheter-related infectious complications were most commonly seen within the first 1,000 HPN days, which

is a reflection of patients' learning curve for catheter care, as previously reported by other authors.¹⁹

Among the catheter-related mechanical complications, occlusion is the most prevalent one.²⁰ This complication may be caused by deposition of fibrin, lipids or drugs infused through the catheter and/or calcium-phosphorus precipitation. Occlusion may be either total or partial, thereby it may be symptomatic or asymptomatic. In the present study, occlusion rate was 0.07/1,000 HPN days, which is lower than that reported in the literature (0.071 occlusions/catheter/year).⁷ Of note, another remarkable catheter-related non-infectious complication is the central venous thrombosis, which in our series yielded a rate similar to that reported in the literature.^{21,22}

The most efficient preventive strategy for catheter occlusion is washing with normal saline after use. We did not find any differences in the tunneled catheter-related complication rate following the introduction of saline sealing as a standard practice, thereby we are not in a position to provide convincing data to determine whether or not tunneled catheters should be heparinized, because such data collection would have required a different study design. We did corroborate that, as reported elsewhere,²³ catheter infection is a risk factor for occlusion.

Liver disease is a major parenteral nutrition metabolic complication.¹² The prevalence of liver abnormalities (e. g. steatosis, cholestasis) in the HPN series from 1970s has been reportedly high, with 25-100% of patients being affected and progressing to advanced liver disease (i. e. cirrhosis, liver failure) in 15-40% of cases. HPN-associated liver disease has declined in most recently reported series,⁷ as is the case in ours. In the present study, a relationship between this complication and the underlying condition or bowel rest (i. e., patients with no oral intake) was not found; however, this association has been reported by other authors.²⁴ This discrepancy is likely to be due to the low liver disease incidence in our series. On the contrary, we did find a relationship of liver disease to HPN length.²⁵ In recent studies, the use of lipid solutions containing 3 fatty acids has resulted in both decreased liver disease incidence and improved clinical evolution.^{26,27}

Metabolic bone disease (MBD) is a common HPN complication.¹¹ In our series, only 18.7% of patients had a density bone test done, which prevents drawing any conclusions about the actual prevalence of this complication. The results from studies with long-term follow-up reported in the literature suggest that metabolic bone disease may affect 84% of patients (43% osteopenia, 41% osteoporosis and 10% pathologic fracture).²⁸ In our series, we found a consistent relationship between MBD and its well-established risk factors, such as gender and lacking physical activity. The role of HPN in bone mass loss remains unknown. HPN-associated bone mass loss is thought to be of multifactorial origin, and it is likely to greatly depend on the underlying condition causing intestinal failure.²⁹

Improving quality of life of patients during HPN is becoming increasingly important, as suggested by the growing interest of authors in research on HPN-related life quality.^{14,30} In the present study, only 18.8% of patients on HPN had normal activity, which is consistent with findings from other studies.³¹

Our study shows that HPN resulted in a mean survival longer than 11 years in patients with underlying conditions other than cancer, which is similar to findings in other European and USA series.^{13, 32} This comes to confirm the HPN role as a first line therapy for chronic intestinal failure. In the present investigation, the diagnosis (i. e. the underlying condition) turned out to be the only independent variable that significantly influenced survival.

The major drawbacks of our study are all related to the retrospective design and the excessive length of the time period covered. The comparative analysis of the HPN complications that had been emerging within the different time periods covered in our study following the implementation of certain measures (e. g. the switch to lipid solution, sealing of tunneled catheters with normal saline) is a reflection of our own learning curve for the prevention, control and management of such complications, as described in previous reports.^{20,33} Furthermore, additional changes have been being introduced in our clinical practice over time that may have had a significant impact on HPN complications in a manner that we were not able to control in the present study, including the canalization of central venous catheters by the interventional radiologist under ultrasound/radiological control in replacement of blind puncture or dissection performed by the surgeon or the change in the antiseptic solution by switching to chlorhexidine. These changes may have contributed to the overall good clinical outcomes found in our series.

Given the low prevalence of both intestinal failure, similar to that of rare diseases, and HPN, it is recommended that such patients be treated at reference medical centres by a highly experienced multidisciplinary team in order to reduce complication rate and improve survival.^{15,20,34}

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Original / Investigación animal

Assessments of body composition and bone parameters of lactating rats treated with diet containing flaxseed meal (*Linum usitatissimum*) during post-weaning period

Danielle Cavalcante Ribeiro, Paula Cristina Alves da Silva, Aline D'Ávila Pereira, Bianca Ferolla da Camara Boueri, Carolina Ribeiro Pessanha, Máira Duque Coutinho de Abreu, Henrique Saldanha Melo, Leticia Rozeno Pessoa, Carlos Alberto Soares da Costa, Gilson Teles Boaventura

Laboratory of Experimental Nutrition. Departament of Nutrition and Dietetics. Fluminense Federal University. Rio de Janeiro. Brazil.

Abstract

Introduction: There are few studies on body composition and the effects of diet on weight postpartum women. The aim was to evaluate the body composition and bone parameters in lactating rats treated with diet containing flaxseed flour during postweaning period.

Methods: After weaning, the lactating rat were divided in control (n = 6) and experimental (F, n = 6) group, treated with 25% flaxseed flour diet. After 30 days, body composition by dual-energy X-ray absorptiometry, serum analysis, organs and intra-abdominal fat mass, femur and lumbar vertebra parameters were determined.

Results: The groups showed similar food intake, body mass and bone parameters. While F group showed the following: lower body (-5%), gonadal (-17%), mesenteric (-23%) and intra-abdominal (-6%) fat mass. Increase of HDL-cholesterol (+10%) and lower glucose (-15%), triglycerides ($P < 0.05$, -37%) and cholesterol ($P < 0.05$, -21%).

Conclusions: The findings highlight the effects of flaxseed for control of adiposity and to maintain a healthy biochemical profile during the postnatal period.

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Key words: *Flaxseed flour. Rats. Postweaning period. Adiposity. Bone.*

EVALUACIONES DE COMPOSICIÓN CORPORAL Y PARÁMETROS ÓSEOS EN RATAS LACTANTES TRATADAS CON DIETAS A BASE DE LINAZA (*LINUM USITATISSIMUM*) DURANTE EL PERIODO DE DESTETE

Resumen

Introducción: Hay pocos estudios sobre la composición corporal y los efectos de la dieta en mujeres en el periodo postparto. El objetivo consistió en evaluar la composición corporal y los parámetros óseos en ratas lactantes tratadas con dietas a base de linaza durante el periodo de destete.

Métodos: Después del destete, las ratas lactantes fueron divididas en un grupo de control (n = 6) y un grupo experimental (F, n = 6), tratadas con una dieta a base de harina de lino al 25%. Al cabo de 30 días, se midieron los parámetros corporales mediante absorciometría de rayos X de doble energía, se realizó un análisis sérico, y se evaluó órganos y masa grasa intra-abdominal así como los parámetros en fémur y vértebras lumbares.

Resultados: El grupo mostró una ingesta alimenticia similar, así como parámetros óseos y de masa corporal. Mientras que el grupo F mostró los porcentajes siguientes en masa grasa: parte inferior del cuerpo (-5%), gonadal (-17%), mesentérica (-23%) e intra-abdominal (-6%). Aumento de HDL-colesterol (+10%) y disminución de glucosa (-15%), triglicéridos ($P < 0,05$, -37%) y colesterol ($P < 0,05$, -21%).

Conclusiones: Los resultados destacan los efectos del lino para el control de la adiposidad y para mantener un perfil bioquímico sano durante el periodo postnatal.

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Palabras clave: *Harina de lino. Ratas. Periodo pos-destete. Adiposidad. Huesos.*

Correspondence: Gilson Teles Boaventura.

Laboratory of Experimental Nutrition.
Departament of Nutrition and Dietetics.
Fluminense Federal University.
Rio de Janeiro. Brazil.
E-mail: gilsontb@gmail.com

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Introduction

According to the World Health Organization (WHO), there are periods of life considered vulnerable to the development of future obesity, as women in the reproductive period, with successive pregnancies.¹ The period of pregnancy and lactation are phases that produce a redirection of nutrients to the maternal tissues. The relationship between pregnancy and changes in adipose tissue was analyzed in a longitudinal study in which the results indicated that there is an association between pregnancy and increased adiposity in women.^{2,3} Reports and studies of women with severe obesity have pointed to pregnancy as a cause of their excess weight.⁴

It is too often mothers face challenges related to changes common to postpartum period, such as weight gain, decreasing levels of physical activity and increased food consumption.⁵⁻⁷ Furthermore, during pregnancy occur changes in bone physiology to compensate for the increasing needs of minerals and developing fetuses. During lactation, there is an increase in the rate of bone resorption, and loss of calcium from the skeleton feeding. Although the rate of bone formation is increased during this time, is exceeded by the rate of bone resorption, resulting in a rapid decrease in bone mass.⁸ However, there are few studies on body composition and the effects of diet on weight postpartum women.

Preventive and therapeutic strategies, including nutritional interventions are possible ways to avoid the appearance of changes in metabolism.^{2,9} In this context, flaxseed (*Linum usitatissimum*) has distinguished between the effects foods with disease prevention, in addition to being an adjunct in combating obesity and overweight.^{10,11}

Flaxseed (*Linum usitatissimum*) is made up of 41% lipids (50-55% as α -linolenic acid, and 15-18% as linoleic acid), 28% fibers, 21% protein, 4% minerals and 6% carbohydrates distributed among phenolic acids, sugars, lignan and hemicelluloses.¹² Previous studies showed protective effect of flaxseed intake in experimental models.¹³⁻¹⁶ Nevertheless, there is a lack of data on the lactating rats. Thus, the aim of this study was to evaluate the body composition and bone parameters in lactating rats treated with diet containing flaxseed flour during postweaning period.

Materials and methods

The protocol used to deal with experimental animals was approved by Ethics Committee on Animal Research of Fluminense Federal University, Niteroi-RJ, Brazil. All procedures are in accordance with the provisions of Brazilian Society of Science and Laboratory's Animals.

Wistar rats were kept in a room with controlled temperature ($23 \pm 1^\circ\text{C}$) and with an artificial dark-light

Table I
Composition of experimental diets

<i>Ingredient (g/100 g)</i>	<i>C</i>	<i>F</i>
Casein	14.0	8.0
Flaxseed flour	–	25.0
Cornstarch	62.07	52.07
Sucrose	10.0	10.0
Soybean oil	4.0	–
Fiber	5.0	–
AIN-93M Mineral Mix	3.5	3.5
AIN-93 Vitamin Mix	1.0	1.0
L-Cystine	0.18	0.18
Choline Bitartrate	0.25	0.25

C: Control group; F: Experimental group fed with diet containing 25 g/100 g of Flaxseed flour.

Casein, Mineral and Vitamin Mix, L-Cystine and Choline Bitartrate: Pragsoluções®; Cornstarch and Fiber: FARMOS®; Soybean: Liza®; Commercial Sucrose: União®; Flaxseed: Armazen®.

Formulated to meet the American Institute of Nutrition AIN-93M recommendation for rodent diets.¹⁸

cycle (lights on from 07:00 to 19:00 hours). Virgin female rats (3 months old) were caged with male rats and after mating each female was placed in an individual cage with free access to water and food. Within 24h of birth excess pups were removed, so that only six pups were kept per dam. This procedure maximizes lactation performance.¹⁷ During 21 days of lactation, rat dams were continued on an *ad libitum* diet of standard laboratory food (Nuvilab®, Paraná, Brazil).

After the 21 days of lactation, at weaning, the lactating rat were randomized divided in control (C, n = 6) and experimental (F, n = 6) group. Both groups were treated with semi-purified diet based on American Institute of Nutrition (AIN-93M) recommendations.¹⁸ The control diet containing 14 g of casein, 4 ml of soybean oil and 5 g of fiber/100 g. While the experimental diets containing 8 g of casein and 25 g of flaxseed flour. The groups received the same amounts of vitamins and minerals per gram of diet (table I). The flaxseeds were crushed to obtain the flour that was weighed and used immediately for the diet preparation. The experimental diet had a concentration of 25% of flaxseed that aimed to meet the entire recommended fiber intake and it was not necessary to add oil because this seed is source of this component. Food intake (g) and body mass (g) were evaluated every 3 days. The female rats had free access to diet and water.

At the end of the nutritional period, 30 days post-weaning, after 8 h of fasting, rats were anesthetized with Thiopentax® (*Tiopental*, 0.1 mg/100 g) and subjected to dual-energy X-ray absorptiometry (DXA)^{19,20} using a Lunar IDXA 200368 GE instrument (Lunar, Wisconsin, USA) with specific software (encore 2008. Version 12.20 GE Healthcare). Total lean (g), fat mass (g), and bone analysis (bone mineral density- BMD (g/cm²); bone mineral content- BMC

(g); and bone area (cm²)) were measured for each rat. The DXA technician did not know about the experimental protocol.

After DXA, the length (cm, measured as the distance from tip of the nose to the tip of the tail) was evaluated. And blood was collected by cardiac puncture. Blood samples were centrifuged and serum was stored at -80° C for posterior analyze of glucose, triglycerides, cholesterol, HDL-cholesterol, calcium, phosphorus, magnesium (mg/dL, respectively) and albumin (g/dL) by colorimetric method (Bioclin BS-120, Belo Horizonte, MG, Brazil). Liver, heart, kidney, pancreas and intra-abdominal fat mass (retroperitoneal, mesenteric and gonadal) were excised and weighted (g).

Right femur and lumbar vertebra (LV4) were collected and cleaned of soft tissue and preserved at -80° C for posterior analyze. Bone dimension: the distance between epiphysis and the medial point width of the diaphysis were measured using calipers with a readability of 0.01mm. After drying overnight, femur and LV4 were weighed. Before, bone mineral density (BMD), in each femur and LV4, was determined by DXA.²¹ After DXA analyses the bones were carried out in order to make the mineral composition where the bone samples were dried at 105° until reaching stable weight, then it were submitted to higher temperatures to 550° in Muffle Quimis Microprocessor - Q318M until they become ashes and liquefied them in thermostat at 80° with nitric acid to 70% in order to analysis minerals of calcium, phosphorus and magnesium by colorimetric method (Bioclin, Belo Horizonte, MG, Brazil).

Statistical analyses were carried out using the Graph Pad Prism statistical package version 5.00, 2007 (San Diego, CA, USA). Food intake and body mass were analyzed by two-way ANOVA, followed by Bonferroni post-test. The other data were analyzed by Student's *t* test. All results are expressed as means $\pm$ SEM with significance level of 0.05.

Results

During the nutritional period, food intake and body mass no differs between groups. In regard to body length, control (41.05 $\pm$ 0.63 cm) and experimental (42.42 $\pm$ 1.37 cm) groups showed no significantly differences in the end of experimental period (fig. 1).

In regard to body composition, total lean, body BMD, BMC and bone area the groups showed similar results. Meantime, the experimental group showed lower fat mass (-5%) to control (table II).

When evaluated the organs mass at 30 days post-weaning, liver, heart, kidney and pancreas mass were similar between control and experimental groups. The adiposity showed lower gonadal (-17%) and mesenteric (-23%) and intra-abdominal (-6%) fat mass in the experimental group (table III).

Serum analyzes showed no differences to calcium, phosphorus, magnesium and albumin. However, the

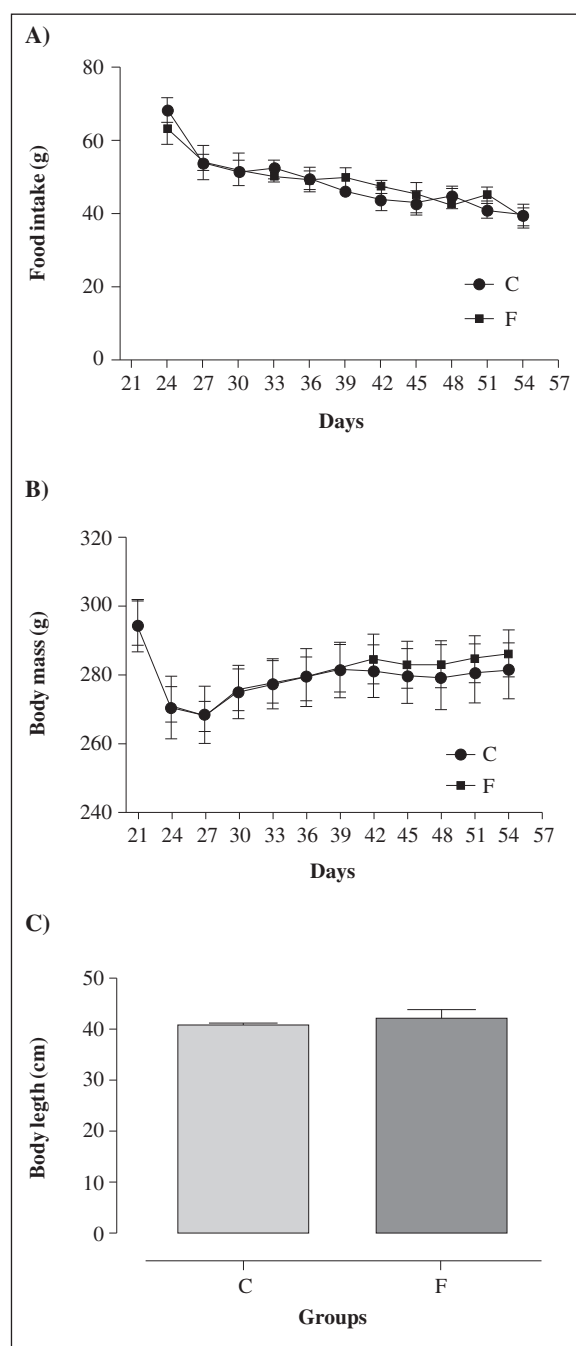


Fig. 1.—Food intake (A) and body mass (B) of lactating rats during 30 days post-weaning. Body length (C) in the end of experimental period. Control group, fed with control diet (○, C, n = 6) and experimental diet, containing 25 g/100 g of flaxseed flour (●, F, n = 6). Values are means (A and B, twoway ANOVA. C, Student's *t* test).

experimental rats showed increase of HDL-cholesterol (+10%) and smaller glucose (-15%), triglycerides ($P < 0.05$, -37%) and cholesterol ($P < 0.05$, -21%) compared to control group (table IV).

Femur and lumbar vertebra (LV4) analyzes showed no differences to mass, bone dimensions and bone mineral density. When evaluated the bone mineral composition in femur and lumbar vertebra, the groups

Table II
Body compartments analyzed by DEXA, at 30 days post-weaning

	C (n6)		F (n6)	
	Mean	SEM	Mean	SEM
Total lean (g)	176.20	2.86	182.30	4.63
Fat mass (g)	79.50	7.02	75.17	6.60
Body BMD (g/cm ²)	0.15	0.01	0.15	0.01
Body BMC (g)	8.38	0.32	8.15	0.25
Body bone area (cm ²)	52.83	1.07	53.00	0.96

C: Group fed with control diet; F: Group fed with experimental diet, containing 25 g/100 g of flaxseed flour. Values are means (Student's t test).

Table III
Organ and intra-abdominal fat mass (g) at 30 days post-weaning

	C (n6)		F (n6)	
	Mean	SEM	Mean	SEM
Liver	8.31	0.66	7.93	0.53
Heart	1.40	0.35	1.47	0.43
Kidney	1.32	0.37	1.22	0.36
Pancreas	2.37	0.50	2.08	0.57
Retroperitoneal fat	4.21	0.56	5.51	1.19
Gonadal fat	7.83	0.98	6.46	0.80
Mesenteric fat	4.24	0.46	3.23	0.28
Intra-abdominal fat	16.29	1.88	15.21	2.01

C: Group fed with control diet; F: Group fed with experimental diet, containing 25 g/100 g of flaxseed flour. Values are means (Student's t test).

showed no differences to calcium, phosphorus and magnesium concentrations (table V).

Discussion

To our knowledge, this study to evaluate the effects of diet containing flaxseed flour on the maternal physiology after lactation in rats. Our results showed that, associated with a significant reduction in the serum cholesterol and triglycerides, the flaxseed flour intake contributes to control of body and intra-abdominal adiposity.

The nutritive demands of lactation are considerably greater than those of pregnancy. The nutrient intake of lactating women affects the nutrient content of breast-milk and maternal health. Thus, nutritional requirements for lactating women are higher compared to women who do not breastfeed.^{2,22} However, there is little information that evaluates the nutrient intake and body composition of women after lactation period. In the present study, both groups received diet based on AIN-93M, to be used during adult maintenance.¹⁸ And

Table IV
Serum analytes at 30 days post-weaning

	C (n6)		F (n6)	
	Mean	SEM	Mean	SEM
Glucose (mg/dL)	166.20	16.82	140.70	12.34
Triglycerides (mg/dL)	75.80	11.67	47.50*	1.50
Cholesterol (mg/dL)	55.67	2.60	43.67*	2.01
HDL-Cholesterol (mg/dL)	19.83	0.94	21.83	1.66
Calcium (mg/dL)	11.30	0.36	11.38	1.50
Phosphorus (mg/dL)	6.70	0.43	6.86	0.40
Magnesium (mg/dL)	2.68	0.09	2.71	0.11
Albumin (g/dL)	3.58	0.04	3.40	0.08

C: Group fed with control diet; F: Group fed with experimental diet, containing 25 g/100 g of flaxseed flour. Values are means.

*Significantly different from the control group (Student's t test, P < 0.05).

Table V
Femur and LV4 mass, dimensions, bone mineral density (BMD) and bone mineral composition at 30 days post-weaning

	C (n6)		F (n6)	
	Mean	SEM	Mean	SEM
Femur:				
Mass (mg)	737.30	32.59	681.10	35.61
Distance between epiphysis (mm)	141.80	20.23	140.60	16.07
Width of the diaphysis (mm)	162.00	3.46	163.70	3.75
BMD (g/cm ²)	0.16	0.004	0.15	0.003
Calcium (mg/dL)	29.28	0.27	28.98	0.80
Phosphorus (mg/dL)	6.67	0.31	6.55	0.18
Magnesium (mg/dL)	15.29	0.96	13.75	0.96
LV4:				
Mass (mg)	219.30	11.25	206.30	16.88
BMD (g/cm ²)	0.14	0.005	0.13	0.004
Calcium (mg/dL)	18.43	0.50	18.15	0.67
Phosphorus (mg/dL)	4.79	0.45	6.01	0.56
Magnesium (mg/dL)	3.82	0.80	3.14	0.93

C: Group fed with control diet; F: Group fed with experimental diet, containing 25 g/100 g of flaxseed flour. Values are means (Student's t test).

to our surprise, regardless of flaxseed meal in the experimental diet, the groups showed similar food intake and body mass development. Previous studies related that the presences of fibers from flaxseed, as their bioactive compounds, are able to promote the satiety sensation, helping to reduce body mass.^{14,23} Nevertheless, seems that the diet containing flaxseed did not affect satiety and the balance of the body mass, in the post-lactation period.

Excessive weight gain during pregnancy and retention of weight in the post-partum period are risk factors for obesity in later life.^{24,25} Strategies to prevent post-partum obesity include behaviors associated with

improved diet and weight control.²⁶ In present study, the fat tissue analyzes, highlighted a lower percentage of body, gonadal, mesenteric and intra-abdominal fat mass in the female rats treated with experimental diet. Flaxseed contain relevant concentration of lipids, and previous studies support the concept that fats do not affects body fat compartments equally.²⁷⁻²⁹ Thereby, the flaxseed flour intake may be associated with a decrease of adipose mass in body and intra-abdominal compartments.

In regard to bone structure, during lactation there is an increase in the rate of maternal bone resorption and in calcium losses from the maternal skeleton. However, when offspring are weaned and milk production is halted, the bone mineral density (BMC) recovers by ~6 months after lactation. In the experimental models, BMC returns to the prepregnancy baseline value after 2-3 weeks in mice,³⁰ 2-6 weeks in rats.^{31,32} Nevertheless, the multi-parity and lactation were risk factors for osteoporosis.^{8,32,33} Several studies have documented the link between the intake of dairy foods and osteoporosis and indicate that polyunsaturated fatty acids may influence bone health.^{21,34-36} The flaxseed contains high concentration of α -linolenic acid and some studies have reported a bone protective effect of this fatty acid; whereas, others have reported no effect.³⁷⁻⁴⁰ The body composition, femur and lumbar vertebra (LV4) analysis demonstrated that female rats of the experimental group followed during ~4 weeks (30 days) after lactation, probably showed the bone parameters recovery regardless of the flaxseed flour.

Among the women, the cardiovascular diseases are responsible for almost half of deaths. Pregnancy brings a physiological stress that can uncover an underlying propensity for chronic diseases, addition to osteoporosis. Thus, the access to postnatal care constitutes a good opportunity for disease prevention.^{41,42} In this context, the diet containing flaxseed flour contributed to the reduction of cholesterol and triglycerides. Although no significant differences have been observed, the experimental group showed higher HDL-cholesterol and lower glucose serum concentration. The findings corroborate previous reports^{12,23} that whole flaxseed contributes to the health lipid profile in hyperlipidemic subjects and in rats with normal biochemical parameters, reducing risks for chronic diseases.

In summary, despite of preliminary analysis, this study described the changes in body composition, bone structure and growth of maternal rats after weaning. Furthermore the findings highlight the contribution of flaxseed flour intake for control of adiposity and to maintain a healthy biochemical profile during the post-natal period.

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Original / Ancianos

Densidad mineral ósea, calcio dietético y factores presuntivos de riesgo de osteoporosis en mujeres ecuatorianas de la tercera edad

Sarita Lucila Betancourt Ortiz

Doctora en Nutrición y Dietética. Máster en Nutrición Clínica. Docente Facultad de Salud Pública. Escuela Superior Politécnica del Chimborazo. Nutricionista. Hospital de Especialidades San Juan. Riobamba. Chimborazo. República del Ecuador.

Resumen

Justificación: La osteoporosis es causa de fracturas patológicas y pérdida de autonomía y validismo en la mujer post-menopáusica. La identificación de factores de riesgo puede servir en la prevención de la aparición de esta co-morbilidad.

Objetivos: Determinar la asociación entre la desmineralización ósea y características demográficas, clínicas y antropométricas selectas de la mujer post-menopáusica que puedan asumirse como factores de riesgo.

Diseño del estudio: No experimental, transversal, analítico.

Serie de estudio: 53 mujeres con edades ≥ 60 años atendidas en el Hospital "San Juan" de Especialidades de Riobamba (Provincia del Chimborazo, República del Ecuador).

Material y método: Se determinó la densidad mineral ósea (DMO) en 2 regiones de interés (columna lumbar | fémur) mediante DEXA (DPX-L, Lunar Technologies, EEUU). La desmineralización ósea se estableció ante puntajes "t" $< -1,0$ desviaciones estándar. La cuantía y calidad de los ingresos de Calcio dietético se estimaron mediante el puntaje pCa que tiene en cuenta la frecuencia de consumo de alimentos tenidos como fuente de calcio y la biodisponibilidad del mineral. Se evaluaron la naturaleza y la fuerza de la asociación entre la desmineralización ósea, por un lado, y los factores presuntivos de riesgo de osteoporosis y el estado del ingreso del calcio dietético, por el otro.

Resultados: La desmineralización ósea fue dependiente de la región de interés: **Fémur:** Osteoporosis: 13,2% + Osteopenia: 50,9%; **Columna lumbar:** Osteoporosis: 49,1% + Osteopenia: 37,7%. Los mayores ingresos de calcio dietético se concentraron en: Leche y lácteos (pCa = 26,56), Carnes, pescados, mariscos y huevos (pCa = 6,51), Frijoles y otras leguminosas (soja incluida) (pCa = 2,85); y Verduras (pCa = 2,54); respectivamente. El puntaje "t" de DMO se asoció con la edad de la mujer, los anteceden-

BONE MINERAL DENSITY, DIETARY CALCIUM AND RISK FACTORS FOR PRESUMPTIVE OSTEOPOROSIS IN ECUADORIAN AGED WOMEN

Abstract

Rationale: Osteoporosis is a cause for pathological fractures and loss of autonomy and validism in the post-menopausal woman. Identification of risk factors might serve for preventing the appearance of this co-morbidity.

Objectives: To determine the association between loss of bone mineral density (BMD) and selected demographic, clinical and anthropometric features in the post-menopausal woman that can be assumed as risk factors of osteoporosis.

Study design: Non-experimental, cross-sectional, analytical.

Study serie: 53 women with ages ≥ 60 años assisted at the "San Juan" Specialities Hospital in Riobamba (Province of Chimborazo, Republic of Ecuador).

Materials and methods: BMD was determined in 2 regions of interest (lumbar spine | femur) by means of DEXA (DPX-L, Lunar Technologies, USA). Loss of BMD was established with "t"-scores < -1.0 standard deviations. Amount and quality of dietetic Calcium intakes were estimated by means of pCa score that takes into account frequency of consumption of foods regarded as sources of calcium and mineral bioavailability. Nature and strength of association between loss of BMD, on one hand, and presumptive risk factors of osteoporosis and state of dietetic calcium intake, on the other, were assessed.

Results: Loss of BMD was dependent upon region of interest: **Femur:** Osteoporosis: 13.2% + Osteopenia: 50.9%; **Lumbar spine:** Osteoporosis: 49.1% + Osteopenia: 37.7%. Highest intakes of dietetic calcium concentrated among Milk and dairy products (pCa = 26.56), Meat, poultry, fish, seafood and eggs (pCa = 6.51), Beans and others legumes (soy included) (pCa = 2.85); and Vegetables (pCa = 2.54); respectively. DMO "t" score associated with woman's age, family history of bone fractures, Body Mass Index (BMI), and body fat (estimated by means of DEXA). Dietetic calcium intakes were independent of presumptive risk factors of osteoporosis and DMO "t" score in the region of interest. Odds-ratios for variables univariately associated with BMD were as follows: **Age:** OR = 2.09 ($p < 0.05$); **BMI:** OR = 0.278 ($p = 0.059$); and **Body fat:** OR = 0.553 ($p > 0.05$); respectively.

Correspondencia: Sarita Lucila Betancourt Ortiz.
Doctora en Nutrición y Dietética. Máster en Nutrición Clínica.
Docente Facultad de Salud Pública.
Escuela Superior Politécnica del Chimborazo.
Nutricionista. Hospital de Especialidades San Juan.
Riobamba. Chimborazo. República del Ecuador.
E-mail: saritabetancourtortiz@yahoo.com.mx

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tes familiares de fracturas óseas, el Índice de Masa Corporal (IMC), y la grasa corporal (estimada mediante DEXA). Los ingresos de calcio dietético fueron independientes de los factores presuntivos de riesgo de desmineralización ósea, y del puntaje "t" de DMO en las regiones de interés. Las razones de disparidades para las variables asociadas univariadamente con la DMO fueron como sigue: Edad: OR = 2,09 ($p < 0,05$); IMC: OR = 0,278 ($p = 0,059$); y Grasa corporal: OR = 0,553 ($p > 0,05$); respectivamente.

Conclusiones: La desmineralización ósea se asocia significativamente con el envejecimiento femenino, y una mayor presencia de la grasa corporal. Los antecedentes familiares de fracturas óseas pueden servir para identificar a la mujer post-menopáusica con un riesgo incrementado de desmineralización ósea. Se deben emprender investigaciones ulteriores para establecer el papel del ejercicio físico y mejores ingresos de calcio dietético como factores protectores de la pérdida de la DMO.

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Palabras clave: *Osteoporosis. Osteopenia. Densitometría mineral ósea. Menopausia. Calcio dietético.*

Introducción

La continua mejoría de los servicios de salud en todo el mundo, unido a cambios en la calidad de vida de las poblaciones humanas, y los superiores estándares de salud, han prolongado la expectativa de vida del ser humano. Consecuentemente, hoy es notorio el crecimiento de las poblaciones de adultos mayores y ancianos. Por lo tanto, cada día hay más personas expuestas a la ocurrencia y progresión, y las consecuencias, de la osteoporosis¹. Es por ello que el interés científico por la osteoporosis ha ganado audiencia en los últimos años².

La osteoporosis es un problema de salud que afecta con particular fuerza al adulto mayor y el anciano³. La pérdida insidiosa de masa mineral ósea conduce a fracturas de sitios anatómicos de relevancia clínica como el cuello de fémur y los cuerpos vertebrales, provocando con ello una fragilidad ósea cada vez mayor, aumento de la morbilidad y la mortalidad, y el deterioro de la calidad de vida del enfermo y sus familiares⁴. Ello significa, a su vez, discapacidad, años de vida perdidos, y necesidad de cuidados; además de los costos elevados de tratamiento y rehabilitación⁵⁻⁶.

Si bien la osteoporosis es una enfermedad asociada a secundaria al envejecimiento, las poblaciones humanas difieren entre sí en cuanto al momento de riesgo incrementado de aparición de esta condición. En el hombre, el riesgo de osteoporosis se incrementa a partir de los 70 años de edad⁷⁻⁹. Sin embargo, el riesgo de osteoporosis en la mujer es mayor durante la menopausia, lo que suele ocurrir entre la quinta y la sexta década de vida¹⁰⁻¹¹.

Las diferencias anotadas para la ocurrencia de osteoporosis según el sexo del individuo también pueden modificar el riesgo de fractura ósea. En ausencia de

Conclusions: Loss of BMD is significantly associated with female aging, and an increased presence of body fat. Family history of bone fractures might serve for identifying post-menopausal women at increased risk of loss of BMD. Further research is required in order to establish the role of physical exercise and better intakes of dietetic calcium as protective factors against loss of BMD.

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osteoporosis, el riesgo de una mujer de sufrir una fractura de cadera en su vida es del 15%, mientras que en el hombre es del 5%¹³. Después de los 50 años de edad, aproximadamente un 40% de las mujeres (en comparación con sólo el 13% de los hombres) puede sufrir una fractura osteoporótica¹³.

La osteoporosis suele afectar a partes importantes de las poblaciones humanas¹⁴⁻¹⁵. En los Estados Unidos, hasta el 20% de las mujeres postmenopáusicas pueden estar afectadas por la osteoporosis¹⁶. Cerca de la tercera parte de las mujeres con edades mayores de 65 años pueden presentar varias fracturas vertebrales, incluso en ausencia de síntomas clínicos¹³⁻¹⁶.

En el Ecuador, el 19% de los adultos mayores de 65 años domiciliados en áreas urbanas sufre de osteoporosis¹⁷⁻¹⁸. El 35% de las mujeres mayores de 45 años sufre de osteoporosis debido a las interacciones que pueden presentarse en la calidad de vida, la actividad física, el consumo de café, el tabaquismo, y la alimentación deficiente durante los primeros 20 años de vida extrauterina¹⁷⁻¹⁸. El 60% de mujeres con edades entre 60 y 69 años, y el 80% de las que tienen de 70 a 79 años, presentan osteopenia¹⁷⁻¹⁸. El 4,8% de las mujeres mayores de 65 años presentan fractura de fémur; pero esta cifra llega a ser del 8,1% en aquellas con edades entre 80-84 años, y del 13,9% en las mayores de 85 años¹⁷. El riesgo de sufrir una segunda fractura de cadera se puede incrementar de 1,6 a 15,0 por 1.000 hombres, y de 3,6 a 22,0 por 1.000 mujeres; respectivamente¹⁷⁻¹⁸.

La desmineralización ósea reconoce la osteopenia y la osteoporosis. La osteopenia es mucho más frecuente que la osteoporosis, pero suele ser menos (re)conocida como factor de riesgo de fractura ósea¹⁹. La osteopenia, más que una enfermedad, constituye para muchos un marcador para el riesgo de fracturas¹⁹.

Aunque la osteopenia pudiera conducir hacia la osteoporosis, la detección temprana de esta condición conlleva la posibilidad del tratamiento para aminorar, detener e incluso revertir la osteoporosis. De aquí la importancia del diagnóstico precoz y el seguimiento sistemático de las distintas formas de la desmineralización ósea en poblaciones que sean identificadas de alto riesgo²⁰.

Se ha avanzado en el conocimiento de la etiopatogenia y la fisiopatología de la desmineralización ósea, y hoy se comprenden mejor los mecanismos normales de regulación de la remodelación ósea, así como las funciones de los osteoblastos y los osteoclastos²¹⁻²². Ello ha abierto nuevas oportunidades para el tratamiento de la osteoporosis²³⁻²⁴. Sin embargo, el diagnóstico temprano, y las estrategias de prevención, son las mejores armas para enfrentar este grave problema de salud pública que representa la osteoporosis²⁵.

Es por todo lo anterior que se ha conducido este trabajo para establecer la relación entre la densidad mineral ósea y factores selectos de riesgo de desarrollo de osteoporosis (entre ellos, los ingresos de calcio dietético) en mujeres menopáusicas. Los resultados alcanzados permitirán contar con información de base para la realización de otros estudios, así como para la implementación de medidas nutricionales correctivas que ayuden en un futuro a disminuir el riesgo de padecer de la desmineralización ósea en cualquiera de sus variantes.

Material y método

Locación del estudio: Hospital de Especialidades "San Juan", de la ciudad de Riobamba, Provincia Chimborazo, República del Ecuador.

Diseño del estudio: Transversal, no experimental, analítico.

Serie de estudio: Fueron elegibles para ser incluidas en el presente estudio las mujeres con edades mayores de 60 años que acudieron al hospital para la medición de la DMO, y que consintieron en participar mediante la firma del correspondiente Acto de Consentimiento Informado.

Las mujeres que se incluyeron finalmente en la serie presente de estudio se seleccionaron mediante muestreo aleatorio simple de entre las elegibles para participar. Se calculó el tamaño de muestra requerido para un 95% de confianza, un valor de α del 5%, y teniendo en cuenta un efecto de diseño de 1,5.

Criterios de inclusión: Edad > 60 años, no reporte de tabaquismo ni de alcoholismo, ausencia de enfermedad crónica que pueda repercutir espuriamente en el estado de la densidad mineral ósea, y ausencia de consumo crónico de fármacos que se conozca interfieran con el metabolismo cálcico (a saber: esteroides y antidepresivos, entre otros).

Criterios de exclusión: Edades ≤ 60 años, tabaquismo y alcoholismo inveterados, presencia de enfermedades relacionadas con el metabolismo óseo: hipo e hipertiroidismo, raquitismo, cáncer, otras enfermeda-

des degenerativas, artritis reumatoidea, consumo crónico de fármacos que interfieren con el metabolismo del calcio (como antidepresivos y corticoides); y negación a participar en el estudio.

El consumo de alcohol se estableció ante el ingreso diario de cantidades de bebidas alcohólicas que excedieran los 40 gramos²⁶. El tabaquismo se estableció ante el consumo diario como mínimo de un cigarrillo, un tabaco torcido, u otros derivados de la hoja²⁷.

De cada mujer se obtuvieron los años de edad cumplidos, la edad de la menarquía, el número de embarazos, la edad de la menopausia (entendida como el cese permanente de la actividad menstrual), los antecedentes personales de fracturas, la presencia de tratamiento corriente de sustitución hormonal, los familiares de osteoporosis, y la práctica de ejercicio físico. La edad se estratificó como sigue: 60-65 años, 66-70 años, 71-75 años, y $+ 75$ años; respectivamente.

El ejercicio físico se definió como la actividad voluntaria realizada por la mujer con un objetivo orientado a la promoción de salud²⁸. La práctica de ejercicio físico se estratificó como sigue: Diaria, 3 veces/semana, 1 vez/semana; y Nunca; respectivamente.

Evaluación antropométrica: Las mujeres fueron talladas y pesadas según protocolos descritos en todas partes²⁹⁻³⁰. Los valores de Talla (en centímetros) y Peso (en kilogramos) se registraron con una exactitud de una décima.

El IMC Índice de Masa Corporal se calculó de los valores corrientes de Talla y Peso. De acuerdo con el valor obtenido del IMC, la serie de estudio se distribuyó en: $< 18,5 \text{ kg/m}^2$: Desnutrición presente; $18,5-24,9 \text{ kg/m}^2$: Bien Nutrida; y $\geq 25 \text{ kg/m}^2$: Exceso de peso; respectivamente.

Medición de la densidad mineral ósea: La Densidad Mineral Ósea (DMO) se midió con un densitómetro DEXA de absorciometría de doble haz LUNAR DPX-L (Lunar Technologies, Estados Unidos) en las siguientes regiones de interés (RDI): columna vertebral lumbar y fémur derecho. Se obtuvieron los valores de DMO de la columna lumbar y el fémur derecho como los t-percentiles de una distribución normal unitaria después de estandarizarlos respecto de la media y la desviación estándar de una población de referencia incluida en el programa de operación del equipo.

Los valores de DMO en las RDI se calificaron según los criterios dados por la Organización Mundial de la Salud (OMS)³¹. La tabla I expone tales criterios.

Medición de la grasa corporal: Como parte del protocolo de medición de la DMO, se obtuvo también el valor de la grasa corporal como la fracción correspondiente de este componente respecto del peso corporal de la mujer. Los valores obtenidos de grasa corporal se estratificaron como sigue: $\leq 35,0\%$; Entre $35,1\%-40,0\%$; Entre $40,1\%-45,0\%$; Entre $45,1\%-50,0\%$; y $> 50,0\%$; respectivamente.

Medición de la frecuencia de consumo del calcio dietético: El estado corriente de la frecuencia de consumo del calcio dietético se estimó mediante un cues-

Tabla I
Criterios empleados para la calificación del valor de densidad mineral óseo obtenido mediante DEXA en la región de interés

Estado	Región de interés	
	Fémur	Columna lumbar
Normal	Puntaje $t > -1,0$ s	Puntaje $t > -1,0$ s
Osteopenia	Entre $-1,0$ y $-2,49$ s	Puntaje $t > -1,0$ s
	Puntaje $t > -1,0$ s	Entre $-1,0$ y $-2,49$ s
	Entre $-1,0$ y $-2,49$ s	Entre $-1,0$ y $-2,49$ s
Osteoporosis	Puntaje $t \leq -2,5$ s	Puntaje $t \leq -2,5$ s

Referencia: [30].

tionario de frecuencia de consumo³². La encuesta le ofreció al sujeto de investigación la posibilidad de registrar el consumo de hasta 15 alimentos diferentes considerados como fuentes de calcio biológico según las frecuencias de consumo siguientes: Diaria, Semanal, Ocasional, y Nunca. De acuerdo con la frecuencia de consumo, se le asignó un puntaje al alimento consumido, como se indica en la tabla II.

Estimación del ingreso de calcio biológico: Los alimentos incluidos en el cuestionario de frecuencia de consumo fueron estratificados según el contenido de calcio dietético en miligramos por cada 100 gramos del alimento³³⁻³⁵, como se muestra en la tabla III. El contenido promedio de calcio dietético en cada grupo de alimento se transformó en una constante de biodisponibilidad después de dividirlo por 100.

La frecuencia de consumo de cada alimento incluido en la encuesta y la constante respectiva de biodisponibilidad se emplearon en el cálculo del pCa como un puntaje indicativo de la cuantía y calidad del calcio dietético ingerido. Brevemente, la frecuencia corriente de consumo se multiplicó por la constante de biodisponibilidad para obtener el pCa propio de cada alimento ($pCa_{\text{Leche_Fluida}} = \text{Frecuencia de consumo} * \text{Constante de biodisponibilidad}$; Si frecuencia de consumo = "Diaria", entonces $pCa = 3 * 4,9 = 14,7$).

Los valores de pCa calculados para cada uno de los alimentos registrados en las encuestas se sumaron para obtener el pCa acumulado propio de cada mujer.

Procesamiento de los datos y análisis estadístico-matemático de los resultados: Los datos demográficos, clínicos y antropométricos de las mujeres, los valores de DMO en cada región de interés, los ingresos de calcio biológico, y los valores acumulados de pCa se registraron en formularios creados *ad hoc*, y se vaciaron en una hoja de cálculo electrónico creada con EXCEL de OFFICE para WINDOWS (Microsoft, Redmon, Virginia, Estados Unidos).

Las variables contempladas en el diseño experimental se redujeron a estadígrafos de locación (media), dispersión (desviación estándar) y agregación (frecuencias absolutas/porcentajes), según fuera el tipo de las mismas.

Se estimó la naturaleza de la asociación entre el valor de la DMO, por un lado, y las variables consideradas como factores presuntivos de riesgo de osteoporosis, por el otro; mediante tests estadísticos de independencia basados en la distribución ji-cuadrado o la distribución t de Student, según fuera el tipo de la variable³⁶. Si ello no fuera posible, la asociación entre las variables de interés se estimó del coeficiente de correlación de Pearson. La fuerza de la asociación univariada se estimó mediante el cálculo de la correspondiente razón de disparidades³⁶. En algunas instancias se empleó el test de Kruskal-Wallis para la dódima de tests de independencia en casos de 3 (o más) estratos l subgrupos de comparación y anticipando un efectivo muestral desigual³⁷. Se eligió un nivel del 5% para denotar las asociaciones observadas como significativas³⁶⁻³⁷.

Las variables que se asociaron univariadamente con el valor de la DMO se incluyeron en una maquinaria de regresión logística ordinal para aislar el efecto "puro" de las mismas, después de controlar las interacciones existentes entre ellas. La fuerza de la asociación entre una variable en particular y el valor de la DMO se estimó de la razón de disparidades devuelta por la regresión logística ordinal ajustada³⁸.

El programa EPI DAT v. 4 (CDC Centros para el Control de las Enfermedades, Atlanta: Estados Unidos) se utilizó para la determinación del tamaño de la muestra del estudio. Los sistemas JMP v. 5 (SAS Institute, Cary, NC) y SPSS v. 20.0 (SPSS Inc., New York) se emplearon en el análisis estadístico de los resultados.

Tabla II
Definición y puntaje asignado a la frecuencia de consumo de los alimentos encuestados en este estudio

Frecuencia de consumo	Definición	Puntaje asignado
Diaria	Consumo de uno (o más) de los alimentos descritos en la encuesta como parte de la dieta diaria del sujeto	3
Semanal	Consumo de uno (o más) de los alimentos 3 veces (como mínimo) en la semana	2
Ocasional	Consumo de uno (o más) de los alimentos cada 15 días (o más)	1
Nunca	Ausencia de la dieta regular del sujeto de los alimentos que aportan calcio biológico	0

Tabla III

Constantes de biodisponibilidad asignadas a los alimentos encuestados en este estudio según el aporte de calcio dietético. La constante de biodisponibilidad propia de cada grupo de alimentos se expresó como una fracción centesimal del contenido promedio de calcio dietético

<i>Grupo</i>	<i>Alimento</i>	<i>Contenido de calcio (mg/100 g)</i>	<i>Constante de biodisponibilidad</i>
Leche, otros lácteos y derivados	Leche fluida	120-1.200	4,90
	Yogurt		
	Queso		
Pescados y mariscos	Pescados	30-400	1,90
	Mariscos		
Huevos	Huevos	80-280	1,79
Frijoles y otras leguminosas	Frijoles	18-103	0,60
	Chochos (<i>Lupinus spp.</i>)		
	Soja		
	Leche de soja		
	Otros productos elaborados con soja		
Frutas	Naranja	12-58	0,34
Verduras	Brócoli	11-192	0,55
	Col		
	Puerro		
	Espinacas		
Nueces y frutos secos	Almendras	61-240	1,53

Referencias: [33]-[35].

Resultados

Fueron elegibles para participar en este estudio 154 mujeres que acudieron al Hospital de Especialidades de Riobamba para la realización de una densitometría ósea mediante DEXA. De ellas, 53 (34,4%) reunieron los criterios de inclusión en el estudio, y por consiguiente, integraron la serie de estudio.

La tabla IV muestra los hallazgos encontrados en cada una de las variables demográficas, clínicas y antropométricas incluidas en el diseño experimental de la investigación. Predominaron las mujeres con edades entre 60-65 años. El número promedio de embarazos en la serie de estudio fue de $4,7 \pm 2,6$. La edad de la menarquía fue de $47,6 \pm 4,6$ años.

La tercera parte de las mujeres estaba tratada con terapias de sustitución hormonal. Casi la mitad de ellas estaba suplementada con calcio + bifosfonatos. Por otro lado, la mitad más uno de las mujeres practicaba ejercicio físico diariamente o 3 veces a la semana.

Solo el 60,0% de las participantes en el estudio presentó fracturas óseas después de los 50 años.

La mitad más uno de las mujeres tenía valores del IMC entre 25,0-29,9 kg/m², mientras que el valor promedio de la grasa corporal fue del $40,9 \pm 5,8\%$.

Según la RDI, la DMO se comportó de la manera siguiente: *Columna lumbar*: $-2,4 \pm 2,4$ [Rango de valores: $-5,1 \rightarrow +1,6$]; y *Fémur*: $-1,7 \pm 0,9$ [Rango: $-4,4 \rightarrow +0,8$]. La figura 1 muestra la frecuencia de trastornos de la mineralización ósea en la serie de estudio según la región de interés.

La tabla V muestra la asociación entre la presencia de desmineralización ósea (Osteopenia/Osteoporosis), estimada del puntaje “t” observado después del análisis DEXA del fémur derecho de la mujer, y las variables incluidas en el diseño experimental del estudio como factores presuntivos de riesgo. La desmineralización ósea se asoció solamente con el IMC (r^2 según Pearson = 0,335; $p < 0,05$; $\chi^2 = 8,54$; $p < 0,05$), y la grasa corporal (r^2 según Pearson = 0,389; $p < 0,05$) de la mujer. La asociación entre la edad de la mujer y la desmineralización ósea fue marginal, a juzgar de los resultados discrepantes del coeficiente de determinación estimado según Pearson ($r^2 = 0,083$; $p < 0,05$) o Spearman ($r^2 = 0,046$; $p > 0,05$).

De acuerdo con los resultados de la encuesta dietética administrada, el 85,5% de las mujeres estudiadas declaró que consumía algún lácteo, sea éste leche, yogurt o queso. Respecto de los otros alimentos incluidos en la encuesta dietética, el 77,5 de las mujeres participantes en el estudio afirmó que consumía mariscos, pescados o huevo; el 93,9% de ellas dijo que ingería chochos (u otros leguminosas); el 35,8% tomaba leche de soja; y el 72,6% comía alguna variedad de las verduras incluidas en la encuesta. Solo el 20,8% de las mujeres consumía naranja; y el 3,8% de ellas almendras.

La figura 2 muestra la distribución de los alimentos encuestados según la frecuencia anotada de consumo. La frecuencia de consumo de un alimento especificado fue independiente del grupo de pertenencia del mismo.

Los valores acumulados de pCa para-todos-los-alimentos en la población estudiada fueron de $39,8 \pm 9,5$

Tabla IV
Características demográficas, clínicas y antropométricas de las mujeres participantes en el estudio presente

Variable	Estratos y frecuencia [%]	Media $\pm$ desviación estándar [Mínimo-Máximo]
Edad, años	60-65 años: 23 [43,4] 66-70 años: 12 [22,6] 71-75 años: 15 [28,3] + 75 años: 3 [5,7]	67,8 $\pm$ 6,1 [60-86]
Número de embarazos		4,7 $\pm$ 2,6 [0-12]
Edad de la menarquia, años		13,9 $\pm$ 1,6 [11-18]
Edad de la menopausia, años		47,6 $\pm$ 4,6 [35-55]
Tratamiento de sustitución hormonal	Sí: 18 [34,0]	
Suplementación con calcio + Tratamiento con bifosfonatos	Sí: 25 [47,0]	
Ejercicio físico	Diariamente: 12 [23,0] 3 veces/semana: 15 [28,0] 1 vez/semana: 9 [17,0] Ninguna: 17 [32,0]	
Fractura ósea después de los 50 años	Sí: 3 [6,0]	
Antecedentes familiares de fracturas	Sí: 10 [19,0]	
Talla, cm		147,0 $\pm$ 5,2 [134,0-59,0]
Peso, kg		61,3 $\pm$ 9,2 [39,0-81,0]
IMC, kg/m ²	Entre 18,5-24,9: 8 [15,1] Entre 25,0-29,9: 28 [52,8] $\geq$ 30,0: 17 [32,1]	28,4 $\pm$ 3,7 [21,5-37,1]
Grasa corporal, %	$\leq$ 35,0%: 6 [11,3] Entre 35,1%-40,0%: 15 [28,3] Entre 40,1%-45,0%: 19 [35,8] Entre 45,1%-50,0%: 11 [20,8] > 50,0%: 2 [3,8]	40,9 $\pm$ 5,8 [22,9-51,6]

Tamaño de la muestra: 53.
Fuente: Registros del estudio.

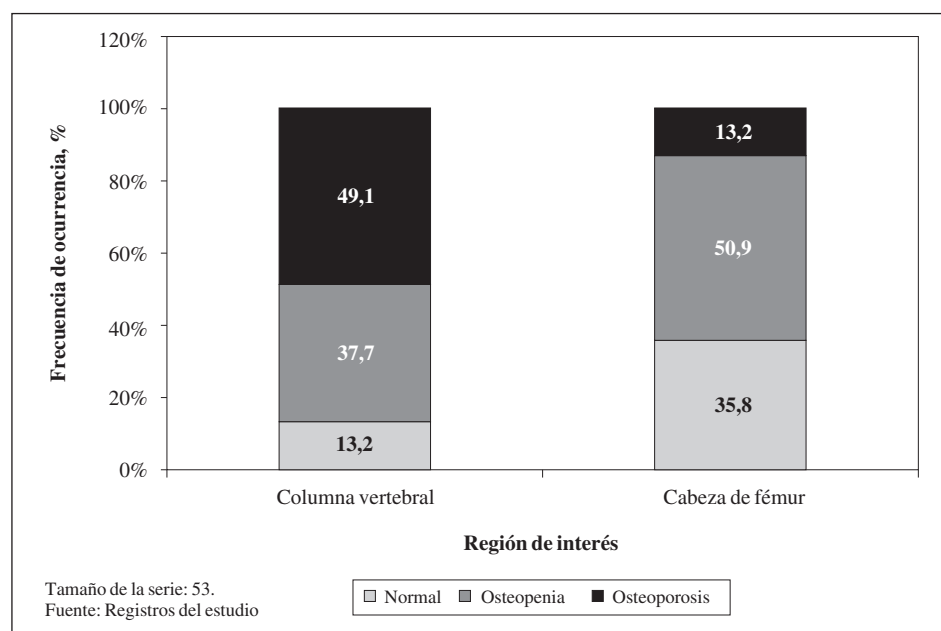


Fig. 1.—Estado de la densidad mineral ósea en las regiones de interés tras la realización del DEXA.

Tabla V
Asociación entre la presencia de desmineralización ósea en el fémur derecho y los factores presuntivos de riesgo de aparición de desmineralización ósea

Característica	Interpretación	
Edad	r^2 (Pearson) = 0,083; $p < 0,05$ r^2 (Spearman) = 0,046; $p > 0,05$	
Edad	60-65 años: 14 [60,9] 66-70 años: 7 [58,3] 71-75 años: 10 [66,7] + 75 años: 3 [100,0]	$\chi^2 = 0,572$; $p > 0,05$
Número de embarazos	r^2 (Pearson) = 0,031; $p > 0,05$ r^2 (Spearman) = 0,003; $p > 0,05$	
Edad de la menarquia, años	r^2 (Pearson) = 0,009; $p > 0,05$ r^2 (Spearman) = 0,003; $p > 0,05$	
Edad de la menopausia, años	r^2 (Pearson) = 0,0003; $p > 0,05$ r^2 (Spearman) = 0,005; $p > 0,05$	
Tratamiento de sustitución hormonal	Sí: 14 [77,8]	$\chi^2 = 2,2$; $p > 0,05$
Suplementación con calcio + Tratamiento con bifosfonatos	Sí: 16 [64,0]	$\chi^2 = 0,0003$; $p > 0,05$
Ejercicio físico	Diario: 7 [58,3] 3 veces/semana: 10 [66,7] 1 vez/semana: 4 [44,4] Ninguna: 13 [76,5]	$\chi^2 = 2,858$; $p > 0,05$
Fractura ósea después de los 50 años	Sí: 3 [100,0]	$\chi^2 = 1,777$; $p > 0,05$
Antecedentes familiares de fracturas óseas	Sí: 9 [90,0]	$\chi^2 = 3,581$; $p > 0,05$
IMC, kg/m ²	r^2 (Pearson) = 0,335; $p < 0,05$ r^2 (Spearman) = 0,347; $p < 0,05$	
IMC	Entre 18,5-24,9: 8 [100,0] Entre 25,0-29,9: 19 [67,9] $\geq 30,0$: 7 [41,2]	$\chi^2 = 8,54$; $p < 0,05$
Grasa corporal, %	r^2 (Pearson) = 0,389; $p < 0,05$ r^2 (Spearman) = 0,250; $p < 0,05$	
Grasa corporal, %	$\leq 35,0\%$: 6 [100,0] Entre 35,1%-40,0%: 11 [73,3] Entre 40,1%-45,0%: 12 [63,1] Entre 45,1%-50,0%: 5 [45,5] $> 50,0\%$: 2 [0,0]	$\chi^2 = 6,73$; $p > 0,05$

Tamaño de la serie: 53.

Fuente: Registros del estudio.

UA [Mínimo: 21,6 UA; Máximo: 62,40 UA]. La figura 3 muestra la distribución de los valores acumulados de pCa obtenidos en la población encuestada según el grupo de alimentos encuestado. Los mayores ingresos de calcio dietético se concentraron en: Leche y lácteos (pCa = 26,6), Pescados, mariscos y huevos (pCa = 6,5), Frijoles y otras leguminosas (pCa = 2,5); y Verduras (pCa = 2,6); respectivamente.

La tabla VI muestra la asociación entre los valores de pCa acumulados para-todos-los-alimentos y los factores presuntivos de riesgo de desarrollo de osteoporosis. Los valores de pCa fueron independientes de los factores incluidos en el diseño experimental como presuntivos de riesgo de desarrollo de osteoporosis.

La figura 4 muestra la relación entre los valores de pCa y la presencia de desmineralización en los sitios anatómicos examinados. Los valores de pCa fueron independientes de la DMO en la región de interés: Valores promedio de pCa: *Columna lumbar*: Densidad mineral ósea conservada: $40,9 \pm 11,5$; Osteopenia: $38,9 \pm 8,8$; Osteoporosis: $40,1 \pm 9,9$ (test de Kruskal-Wallis: $\chi^2 = 0,110$; $p > 0,05$); *Fémur derecho*: Densidad mineral ósea conservada: $36,9 \pm 8,6$; Osteopenia: $42,4 \pm 9,5$; Osteoporosis: $37,6 \pm 10,4$ (test de Kruskal-Wallis: $\chi^2 = 3,359$; $p > 0,05$).

Finalmente, la tabla VII muestra las razones de disparidades estimadas mediante el modelo de regresión logística ordinal construido con las variables incluidas en el

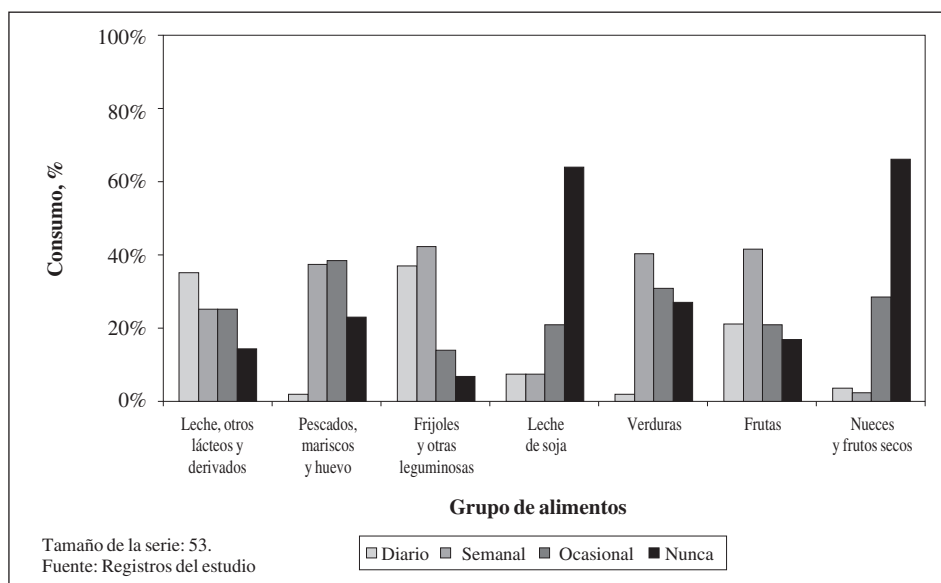


Fig. 2.—Distribución de las frecuencias de consumo de los alimentos incluidos en la encuesta dietética conducida en las mujeres participantes en el presente estudio.

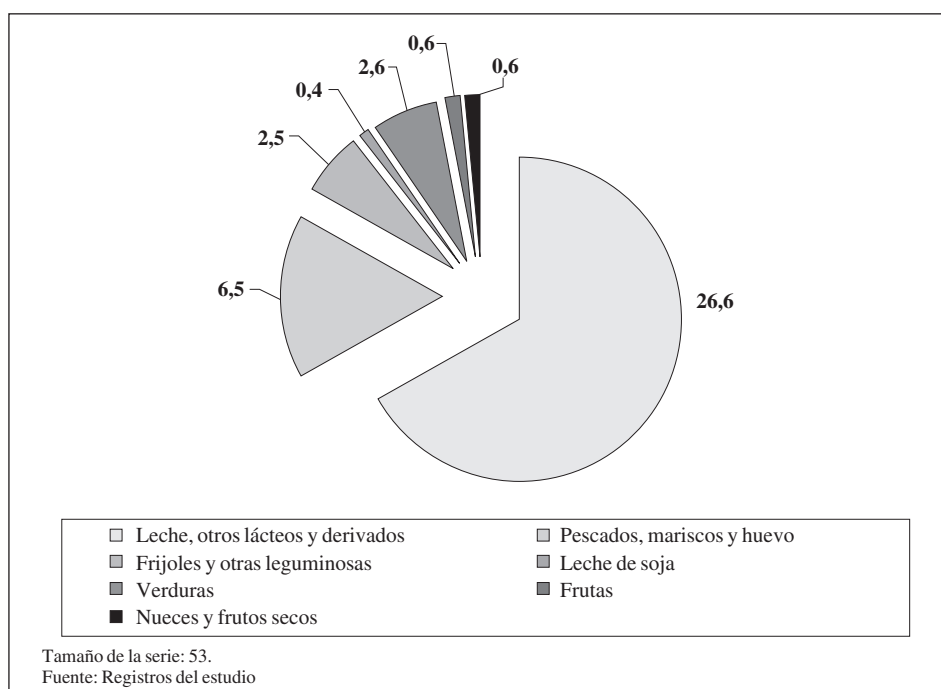


Fig. 3.—Valores de pCa según el grupo alimentario encuestado, pCa denota un puntaje empleado para calificar la cantidad y la calidad de los ingresos de calcio dietético en la serie de estudio.

diseño experimental del estudio presente que se asociaron univariadamente con los valores encontrados de DMO. Se debe hacer notar que la bondad de ajuste del modelo logístico no fue la adecuada ($\chi^2 = 31,771$; $p = 0,788$). No obstante, se observó que la edad del sujeto se asoció con una probabilidad incrementada de ocurrencia de trastornos de la DMO. Esto es, la probabilidad de ocurrencia de trastornos de la DMO se incrementó en 2 veces con cada cambio de estrato de la edad ($\log_{OR} = 0,738$; OR = 2,09; $p < 0,05$; IC 95% = 1,122-3,896).

El IMC ejerció un efecto protector (si bien marginalmente significativo) contra la probabilidad de ocurrencia de trastornos de la DMO. La probabilidad de pre-

sentación de trastornos de la DMO disminuyó en un 72% con cada cambio en la categoría del IMC ($\log_{OR} = -1,278$; OR = 0,278; $p = 0,059$; IC 95% = 0,073-1,052).

Por su parte, el aparente efecto protector de la grasa corporal fue opacado por la pobre significación asociada al valor estimado del OR ($\log_{OR} = -0,591$; OR = 0,553; $p > 0,05$; IC 95% = 0,229-1,333).

Discusión

De acuerdo con este estudio, los trastornos de la DMO estaban presentes en más de la mitad de las muje-

Tabla VI
Asociación entre los valores de pCa y los factores presuntivos de riesgo de aparición de desmineralización ósea

<i>Característica</i>	<i>Interpretación</i>	
Edad	$r^2 = 0,039; p > 0,05$	
Edad [‡]	60-65: $42,0 \pm 8,7$ 66-70: $35,5 \pm 9,7$ 71-75: $41,5 \pm 9,7$ + 75 años: $30,9 \pm 4,9$	$\chi^2 = 7,460^§$ $p > 0,05$
Número de embarazos	$r^2 = 0,006; p > 0,05$	
Edad de la menarquia, años	$r^2 = 0,035; p > 0,05$	
Edad de la menopausia, años	$r^2 = 0,029; p > 0,05$	
Tratamiento de sustitución hormonal [‡]	Sí: 39,8 No: 39,8	t-Student = 0,008; $p > 0,05$
Suplementación con calcio + Tratamiento con bifosfonatos [‡]	Sí: 40,7 No: 39,0	t-Student = 0,624; $p > 0,05$
Ejercicio físico [‡]	Diario: $38,4 \pm 8,1$ 3 veces/semana: $41,1 \pm 10,3$ 1 vez/semana: $41,8 \pm 10,5$ Ninguna: $38,5 \pm 9,8$	$\chi^2 = 1,334^§$ $p > 0,05$
Fractura ósea después de los 50 años ¶	Sí: 34,1 No: 40,1	t-Student = -1,056; $p > 0,05$
Antecedentes familiares de fracturas ¶	Sí: 38,4 No: 40,1	t-Student = -0,506; $p > 0,05$
IMC, kg/m ²	$r^2 = 0,1354; p < 0,05$	
IMC [‡]	Entre 18,5-24,9: $45,2 \pm 12,8$ Entre 25,0-29,9: $40,9 \pm 8,0$ ≥ 30,0: $35,4 \pm 8,9$	$\chi^2 = 5,82^§$ $p > 0,05$
Grasa corporal, %	$r^2 = 0,033; p > 0,05$	
Grasa corporal	≤ 35,0%: $42,3 \pm 13,8$ Entre 35,1%-40,0%: $38,9 \pm 8,3$ Entre 40,1%-45,0%: $43,3 \pm 8,9$ Entre 45,1%-50,0%: $35,7 \pm 7,2$ > 50,0%: $27,5 \pm 8,4$	$\chi^2 = 9,211^§$ $p > 0,05$

[‡]Se muestra en cada estrato la media ± desviación estándar de los valores de pCa.

[§]Estadígrafo de salida del test de Kruskal-Wallis.

Tamaño de la muestra: 53.

Fuente: Registros del estudio.

res posmenopáusicas atendidas en un centro médico especializado de una importante ciudad de los Andes ecuatorianos. En consecuencia, este trabajo se une a otros anteriores para afirmar que la pérdida de la DMO puede afectar a una proporción importante de las mujeres ecuatorianas con edades > 60 años. En el caso particular de la osteoporosis, como forma extrema de la desmineralización ósea, este trabajo encontró que la frecuencia de ocurrencia de la misma fue dependiente de la región de interés, con estimados tan desiguales como un 13% para el fémur derecho, y un 49% para la columna vertebral.

La mayoría de las 1,229.089 personas que viven en el Ecuador con edades > 60 años son mujeres¹⁷⁻¹⁸. Una proporción significativa de las mujeres ecuatorianas postmenopáusicas se concentra en la franja etaria com-

prendida entre los 60 y los 65 años de edad (como se observó en este estudio). Luego, si la osteoporosis no se reconoce e interviene oportunamente, solo queda anticipar un alza epidémica de la fractura ósea en este segmento poblacional, con las consiguientes repercusiones sanitarias, económicas y sociales.

Este trabajo se ha expandido para mostrar las relaciones existentes entre el estado de la DMO en mujeres ecuatorianas post-menopáusicas y varias variables que fueron asumidas como factores presuntivos de riesgo de desarrollo de osteoporosis. De las variables consideradas, fueron solamente la edad de la mujer, el IMC, y la grasa corporal las que se asociaron con los cambios en la DMO observados mediante DEXA en el fémur derecho.

La osteoporosis puede ser una consecuencia del envejecimiento. La desmineralización ósea se inicia

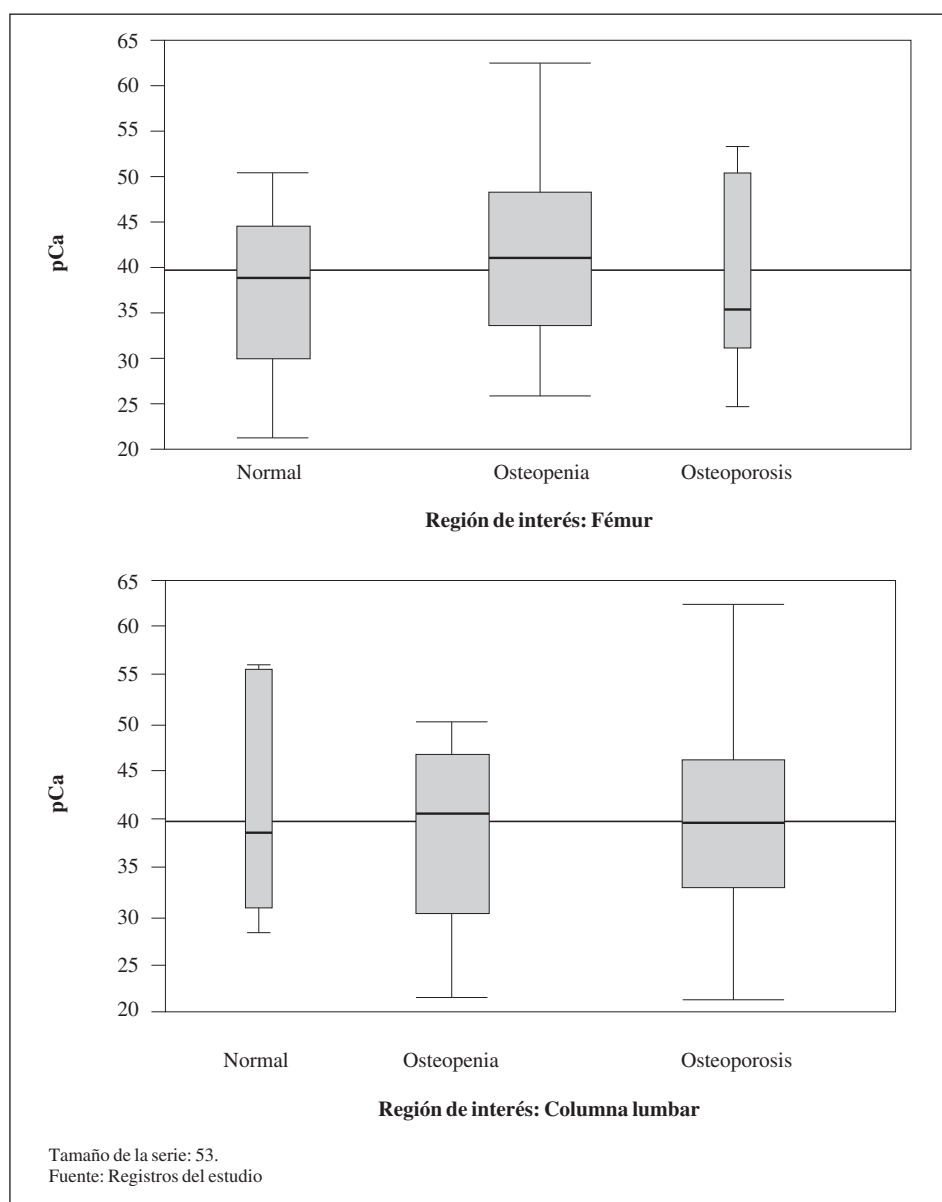


Fig. 4.—Asociación entre el valor del pCa y el diagnóstico de desmineralización ósea en la región de interés. Panel superior: Región de interés: Fémur derecho. Panel inferior: Región de interés: Columna lumbar.

con la supresión de la producción gonadal de estrógenos³⁹⁻⁴⁰, y puede perpetuarse o agravarse con la disminución de la actividad física y el incremento del sedentarismo, los malos hábitos dietéticos, la pobre exposición al sol, y estados malabsortivos que afectan la homeostasis del calcio corporal y la vitamina D^{7-8,10,17-18}. Todo ello resulta en un riesgo incrementado de la mujer postmenopáusica de sufrir fracturas óseas en ocasión de caídas⁴.

Resultó interesante comprobar en este estudio que el IMC, por un lado, y la grasa corporal, por el otro, se asociaron inversamente con los trastornos de la DMO en la muestra estudiada. De hecho, a mayores valores del IMC y la grasa corporal, menor fue la frecuencia de ocurrencia de la desmineralización ósea.

La obesidad ha sido tenida como un factor de riesgo de desarrollo de osteoporosis⁴¹⁻⁴². La sobrecarga mecánica

del exceso de peso corporal sobre los huesos largos de las extremidades inferiores puede conducir al desgaste físico de los mismos, y con ello, la aparición de desmineralización ósea⁴²⁻⁴³. Tampoco se puede pasar por alto que la obesidad se asocia con insulinoresistencia y estados alterados de la utilización periférica de la energía metabólica, y ello puede repercutir sobre el metabolismo óseo y el equilibrio entre la resorción ósea y la formación de hueso nuevo, favoreciéndose entonces la desmineralización ósea⁴⁴⁻⁴⁵. Igualmente, la obesidad induce estados proinflamatorios crónicos que suelen afectar la remodelación ósea, promoviendo la disminución de la DMO⁴⁶⁻⁴⁷.

Sin embargo, el aparente efecto protector de los valores incrementados del IMC en una serie de estudio donde las edades de las mujeres se distribuyeron entre los 60 y los 86 años puede conducir a nuevas interpreta-

Tabla VII
Razones de disparidades e intervalos asociados de confianza al 95%, para los predictores selectos de desmineralización ósea

Variable	$\log_{OR}$	OR
Edad	0,738 (p = 0,020) IC 95% = 0,116-1,360	2,09 IC 95% = 1,122-3,896
IMC	-1,278 (p = 0,059) IC 95% = -2,606-0,051	0,278 IC 95% = 0,073-1,052
Grasa corporal	-0,591 (p > 0,05) IC 95% = -1,471-0,290	0,553 IC 95% = 0,229-1,333

OR: Razón de disparidades; logOR: Logaritmo de la razón de disparidades;
IC: Intervalo de confianza.
Tamaño de la muestra: 53.

Fuente: Registros del estudio.

ciones de la influencia del peso corporal sobre la DMO. El exceso de peso pudiera ser un factor protector ante los cambios que ocurren en la composición corporal que el envejecimiento suele provocar en la composición corporal del anciano. Se ha descrito una mayor actividad física, menor frecuencia de fragilidad, y una mayor supervivencia entre los adultos mayores y ancianos con exceso de peso corporal sin repercusión cardiovascular⁴⁸⁻⁴⁹. El exceso de peso corporal señalaría

a aquellos sujetos con edades > 60 años que se destacan por hábitos dietéticos saludables, y que realizan elecciones alimentarias juiciosas⁴⁹⁻⁵⁰. Luego, el exceso de peso corporal podría servir para contrarrestar el efecto adverso de la edad sobre la DMO.

Valores elevados de la grasa corporal también se asociaron con bajas frecuencias de la desmineralización ósea. Sin embargo, el efecto protector de la grasa corporal en presencia de edades cada vez mayores fue más bien débil (si se juzga de la correspondiente razón de disparidades). Llegado este punto, se debe hacer notar que el término “grasa corporal” engloba varias distribuciones topográficas de este componente molecular, como la grasa retroperitoneal, la grasa visceral, la grasa intraparenquimatosas, y la grasa subcutánea⁵¹⁻⁵². Se ha reportado que los adipocitos presentes en los depósitos subcutáneos de grasa pueden exhibir actividad aromataza, que sería responsable de la aparición en sangre de estrógenos más allá del cese de la esteroidogénesis ovárica⁵³. Entonces, la actividad aromataza de los adipocitos subcutáneos podría servir entonces para preservar la DMO en las edades post-menopáusicas.

Otra línea de evidencia sugiere la mujer con exceso de peso corporal puede absorber y utilizar el calcio dietético con mayor eficiencia⁵⁴. La remodelación ósea en la mujer con exceso de peso corporal es más sensible a la acción de la hormona paratiroidea⁵⁵. Estos mecanis-

Anexo
Distribución del consumo de calcio dietético en la población estudiada. Resultados de la encuesta de frecuencia de consumo administrada a las mujeres participantes en este estudio

Alimento	Frecuencia de consumo			
	Diaria	Semanal	Ocasional	Nunca
<i>Leche, otros lácteos y derivados</i>				
Leche	23 [43,0]	14 [27,0]	8 [15,0]	8 [15,0]
Yogur	6 [11,0]	8 [16,0]	24 [45,0]	15 [28,0]
Queso	27 [51,0]	18 [24,0]	8 [15,0]	0 [0,0]
<i>Pescados, mariscos y huevos</i>				
Mariscos	0 [0,0]	15 [28,0]	28 [53,0]	10 [19,0]
Sardinas	0 [0,0]	4 [8,0]	24 [45,0]	25 [47,0]
Huevo	3 [6,0]	40 [75,0]	9 [17,0]	1 [2,0]
<i>Frijoles y otras leguminosas</i>				
Chochos	5 [9,0]	27 [51,0]	14 [27,0]	7 [13,0]
Leguminosas	34 [64,0]	18 [34,0]	1 [2,0]	0 [0,0]
Leche de soja	4 [8,0]	4 [8,0]	11 [20,0]	34 [64,0]
<i>Frutas</i>				
Naranja	11 [21,0]	22 [41,0]	11 [21,0]	9 [17,0]
<i>Verduras</i>				
Brócoli	1 [2,0]	21 [40,0]	24 [45,0]	7 [13,0]
Col	2 [4,0]	36 [68,0]	12 [22,0]	3 [6,0]
Puerro	1 [2,0]	4 [7,0]	12 [23,0]	36 [68,0]
Espinaca	0 [0,0]	24 [45,0]	17 [32,0]	12 [23,0]
<i>Nueces y frutos secos</i>				
Almendras	2 [4,0]	1 [2,0]	15 [28,0]	35 [66,0]

Tamaño de la muestra: 53.

Fuente: Registros del estudio.

mos, actuando de conjunto, podrían contribuir a la preservación de la DMO en la mujer post-menopáusica.

El diseño experimental de este trabajo incluyó un cuestionario de frecuencia de consumo de alimentos tenidos como fuentes de calcio para evaluar la cantidad y la calidad de los ingresos dietéticos de este mineral. Los mayores ingresos de calcio dietético se concentraron en los lácteos y derivados, los pescados, mariscos y huevos, y las leguminosas. Sin embargo, la frecuencia de consumo de estas fuentes alimentarias de calcio nunca fue mayor del 50%, y, además, se distribuyó desigualmente a través de los distintos grupos alimentarios. Además, no se pudo comprobar asociación alguna entre el estado de los ingresos de calcio dietético (estimado mediante la pCa) y las variables presuntivas de riesgo de osteoporosis.

Está fuera del alcance del diseño de este estudio indagar sobre las causas del desigual ingreso de calcio dietético. El consumo de un alimento en particular es la resultante de un complejo entramado de determinantes económicos, culturales, sociales y personales⁵⁶. La equidad en el acceso al alimento podría determinar la conducta alimentaria de la persona⁵⁷. La disponibilidad del alimento (más allá de los ciclos estacionales de cosecha y producción) también podría influir en el consumo de uno u otro alimento percibido como saludable⁵⁸. La educación alimentaria, el peso de las tradiciones, y las nociones que se tenga sobre la conveniencia de incluir un alimento especificado en el menú diario, también influyen en la historia dietética de la persona⁵⁹.

Se ha recomendado que a partir de los 50 años de edad, la dieta debe aportar diariamente unos 1.500 mg de calcio⁶⁰. Este requerimiento se podría satisfacer del consumo diario de 4 vasos de leche⁶¹. Si ello no fuera posible, la mujer debería ser educada en la elección de otros alimentos que aporten cantidades similares de calcio dietético, como las leguminosas, el huevo, y las nueces y los frutos secos⁶².

Llamó la atención en este estudio el casi nulo consumo de alimentos elaborados con soja. El consumo de una taza de frijol de soja cocido puede brindar más del 20% de los requerimientos diarios de calcio dietético⁶³. Los sucedáneos lácteos de soja son considerados actualmente como una formidable herramienta intervencionista en la osteoporosis⁶⁴. Luego, una mayor promoción del consumo de alimentos elaborados con soja podría servir en la prevención primero, y el tratamiento después, de los trastornos de la DMO en la mujer post-menopáusica.

Se debe reconocer que el envejecimiento trae aparejado trastornos de la absorción intestinal de vitaminas y minerales⁶⁵. Por consiguiente, la suplementación de la dieta regular con sales de calcio debería ser considerada dentro de las estrategias intervencionistas de la osteoporosis en la mujer post-menopáusica⁶⁶.

Conclusiones

De entre una lista de factores presuntivos de riesgo de ocurrencia de trastornos de la DMO, solo la edad, el

IMC, y la grasa corporal se asociaron significativamente con la presencia de osteopenia y osteoporosis en mujeres post-menopáusicas atendidas en un centro especializado de una ciudad de los Andes ecuatorianos. La frecuencia de trastornos de la DMO se incrementó con edades cada vez mayores. Sin embargo, valores elevados del IMC y la grasa corporal se asociaron con frecuencias disminuidas de trastornos de la DMO en la serie de estudio. Se debe hacer notar que el efecto protector del IMC y la grasa corporal fue más bien débil en presencia de valores incrementados de la edad. El consumo de calcio dietético fue independiente de los factores presuntivos de riesgo de osteoporosis.

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Original / Deporte y ejercicio

Relación entre condición física y composición corporal en escolares de primaria del norte de España (Logroño)

Daniel Arriscado¹, José Joaquín Muros², Mikel Zabala³ y Josep María Dalmau¹

¹Dpto. de Ciencias de la Educación. Universidad de La Rioja. Logroño. España. ²Dpto. de Nutrición y Bromatología. Universidad de Granada. Granada. España. ³Dpto. de Educación Física y Deportiva. Universidad de Granada. Granada. España.

Resumen

Introducción: La obesidad infantil es una epidemia que afecta especialmente a los países desarrollados, pero cuyos efectos negativos sobre la salud podrían verse disminuidos por una buena condición física.

Objetivos: El objetivo de este estudio fue determinar el nivel de condición física de una población de escolares de una ciudad del norte de España (Logroño, La Rioja), así como analizar las relaciones del mismo con la composición corporal, la tensión arterial y diversos factores socio-demográficos.

Métodos: El estudio se llevó a cabo sobre una muestra representativa compuesta por 329 escolares de 11-12 años de las 31 escuelas de la ciudad. Se obtuvieron datos socio-demográficos, antropométricos, tensión arterial, desarrollo madurativo y de condición física.

Resultados: Los escolares de género masculino y los normopesos obtuvieron rendimientos superiores en las pruebas de condición física que las chicas y que quienes padecían sobrepeso u obesidad. El 88% de los niños y el 80% de las niñas presentaron valores saludables de capacidad aeróbica, mientras que sólo el 73% de los inmigrantes lo hicieron. Un mayor riesgo de padecer sobrepeso u obesidad se asoció con un menor rendimiento en las pruebas de condición física, encontrándose relaciones inversas entre el porcentaje de grasa y el volumen máximo de oxígeno ($r = -0,524$), la fuerza explosiva del tren inferior ($r = -0,400$) y el rendimiento en velocidad ($r = 0,385$).

Conclusiones: Las relaciones encontradas entre la condición física y la composición corporal ponen de manifiesto la importancia de realizar intervenciones destinadas a mejorar la condición física, especialmente la capacidad aeróbica, haciendo hincapié en los alumnos inmigrantes y de género femenino.

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Palabras clave: Obesidad. Condición física. Composición corporal. Escuela primaria.

Correspondencia: Daniel Arriscado Alsina.

Dpto. de Ciencias de la Educación.

Universidad de La Rioja.

C/ Río Linares, nº 6, 1º C.

26140 Lardero. La Rioja. España.

E-mail: danielarriscado@hotmail.com

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RELATIONSHIP BETWEEN PHYSICAL FITNESS AND BODY COMPOSITION IN PRIMARY SCHOOL CHILDREN IN NORTHERN SPAIN (LOGROÑO)

Abstract

Introduction: Childhood obesity is an epidemic that is more prevalent in developed countries, but the negative effects it has on children's health could be decreased by good physical fitness.

Objectives: The aim of this study was to determine the level of physical fitness of a group of school children in a city in the North of Spain (Logroño, La Rioja), and to analyze the relationship with the body composition, blood pressure and various socio-demographic factors.

Methods: Research was conducted with a representative sample of 329 students aged 11-12 from all 31 schools of the city. Data included their socio-demographic background, anthropometric measurements, blood pressure, biological maturity and physical fitness.

Results: Male students and students with normal body weight fared better in physical fitness tests than females and than those who suffered from overweight or obesity. 88% of boys and 80% of girls were found to have healthy aerobic capacity, while only 73% of immigrant children demonstrated this. A major risk of suffering from overweight or obesity was associated with inferior results in physical fitness tests, finding inverse relationships between the percentage of body fat and maximal oxygen uptake ($r = -0,524$), lower-body explosive strength ($r = -0,400$) and speed performance ($r = 0,385$).

Conclusions: The relationship between physical fitness and body composition demonstrates the importance of intervening in order to improve physical fitness, especially with respect to aerobic capacity, with special emphasis needed for immigrant and female students.

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Key words: Obesity. Physical fitness. Body composition. Primary school.

Abreviaturas

IMC: Índice de masa corporal.

VO2max: Volumen máximo de oxígeno.

Introducción

Los porcentajes de sobrepeso y obesidad infantil han registrado considerables aumentos en los últimos años en los países desarrollados y en vías de desarrollo. En España, más de un 20% de los niños de 10 a 14 años padecen sobrepeso u obesidad¹, lo que resulta especialmente grave teniendo en cuenta las consecuencias negativas para la salud que derivan del exceso de grasa corporal. Entre los principales motivos de esta epidemia destaca la falta de actividad física, uno de los grandes problemas del siglo XXI², de ahí que la Organización Mundial de la Salud³ recomiende un mínimo de 60 minutos diarios de práctica física moderada o vigorosa en los niños de 5 a 17 años.

Diferentes estudios en la población infantil han mostrado los beneficios que la actividad física tiene sobre la composición corporal⁴, los factores de riesgo cardiovascular⁵ y la condición física⁶. Esta última es un factor íntimamente ligado al nivel de actividad física y es definida como la capacidad que una persona tiene para realizar actividad física y/o ejercicio. La condición física comprende cualidades físicas como la capacidad aeróbica, fuerza, resistencia muscular, movilidad articular, velocidad de desplazamiento, agilidad, coordinación y equilibrio. La valoración de estas cualidades se conoce con el nombre de condición física relacionada con la salud, siendo la capacidad aeróbica y la fuerza las que tienen mayor relevancia científico-sanitaria⁷.

Investigaciones recientes confirman que el efecto de la capacidad cardiorrespiratoria es más influyente sobre los factores de riesgo cardiovascular que la propia actividad física⁸. De este modo, se han encontrado relaciones entre la condición física, especialmente en lo referente a la capacidad aeróbica, y los factores de riesgo cardiovascular⁹, la adiposidad corporal¹⁰, la densidad ósea¹¹, la tensión arterial¹² u otros¹³. En cuanto al nivel muscular durante la infancia y la adolescencia, éste ha sido inversamente relacionado con factores de riesgo de enfermedad cardiovascular¹⁴. Además, estos niveles de acondicionamiento muscular parecen perdurar en la edad adulta¹⁵.

Desafortunadamente, a pesar de los beneficios que la práctica física y la condición física reportan sobre la salud, las perspectivas en este sentido no son optimistas, ya que los índices de insuficiente práctica física oscilan entre el 37% de los chicos y el 40% de las chicas en la población escolar española¹⁶, por lo que es necesario definir intervenciones con el objetivo de revertir esta situación.

Objetivos

El objetivo de este estudio fue analizar el nivel de condición física, así como las relaciones entre dicho

nivel y la composición corporal, tensión arterial y factores sociodemográficos en una población representativa de escolares de sexto curso de Educación Primaria (11-12 años) de Logroño.

Métodos

Sujetos

Se diseñó un estudio transversal con una muestra representativa de los alumnos escolarizados en sexto curso de primaria (11,7 años $\pm$ 0,4) de la ciudad de Logroño (La Rioja). De un total de 1.595 alumnos escolarizados para ese intervalo de edad durante el curso 2011-2012, se estimó que el número de escolares necesario para que la muestra fuese representativa era de 310 (intervalo de confianza del 95%). Trescientos setenta y dos escolares fueron seleccionados de manera aleatoria entre los colegios públicos y concertados de la ciudad, de los que 329 aceptaron tomar parte en el estudio.

Todos los alumnos participaron de manera voluntaria y respetando el acuerdo sobre ética de investigación de Helsinki. Se solicitó el consentimiento informado de los padres o tutores de los alumnos. El Comité Ético de Investigación Clínica de La Rioja aprobó este estudio.

Datos sociodemográficos

Los propios participantes en el estudio informaron mediante cuestionario de su sexo, fecha de nacimiento y país de origen. La clasificación de escuelas públicas o concertadas fue facilitada por la Consejería de Educación del Gobierno de La Rioja. El nivel socioeconómico y sociocultural de los alumnos se determinó en función de la información recogida en el Proyecto Educativo del Centro al que asistían, dividiéndolo en las siguientes categorías: medio-bajo, medio y medio-alto.

Medidas antropométricas

Todas las medidas antropométricas fueron tomadas siguiendo el protocolo establecido por la Sociedad Internacional para el Avance de la Cineantropometría¹⁷ y por un único evaluador experimentado, acreditado como nivel II por la citada entidad.

El peso se determinó con una balanza SECA (713, Hamburg, Alemania), con una precisión de 0,1 kg. Para la talla y la talla sentada se empleó un tallímetro Holtain (Holtain Ltd., Dyfed, Reino Unido), con una precisión de 1 mm. A partir de estos datos, se calculó el índice de masa corporal (IMC) como el peso dividido por la altura al cuadrado (kg/m²). En función de este índice, el sexo y la edad de los participantes, se definió el sobrepeso y la obesidad de acuerdo a los puntos de corte internacionalmente establecidos¹⁸. Los perímetros de cintura y cadera fueron medidos con una cinta

de acero flexible Lufkin (Lufkin W606 PM, Michigan, EEUU) de 0,1 cm de precisión. Posteriormente, se calculó el cociente entre cintura y cadera. Se midieron los pliegues cutáneos de tríceps y subescapular con un pliómetro Holtain (Holtain Ltd., Crosswell, Reino Unido), con una precisión de 0,2 mm y una presión constante de 10 g/mm². El porcentaje de masa grasa se estimó mediante las ecuaciones de Slaughter¹⁹.

Maduración sexual

El nivel de maduración sexual fue determinado por investigadores entrenados, del mismo sexo que el alumno y a través de dos procedimientos diferentes:

Por un lado, todos los escolares autoevaluaron el estado madurativo en que se encontraban según la metodología descrita por Tanner²⁰. Por otro lado, se estableció la “edad al pico de crecimiento” mediante ecuaciones que toman como referencia la edad cronológica, el sexo y las siguientes medidas antropométricas: talla, talla sentada, longitud de los miembros inferiores (calculada como la diferencia de las anteriores) y peso²¹.

Presión arterial

Los niveles de presión arterial sistólica y diastólica se determinaron mediante un esfigmomanómetro aneróide Riester (minimus III, Jungingen, Alemania) calibrado y un estetoscopio. Las medidas se realizaron con los alumnos en sedestación, tras más de cinco minutos de reposo previo y con un brazalet adaptado al tamaño del brazo, tal y como indican las recomendaciones internacionalmente aceptadas para la valoración en niños²².

Personal titulado y experimentado fue el responsable de tomar la presión arterial sistólica y diastólica en los dos brazos de cada uno de los participantes. Se registraron las medidas en milímetros de mercurio (mmHg).

Condición física

La condición física se determinó mediante los test de campo de la Batería ALPHA-Fitness²³, a la que se añadió el test de flexión de tronco desde sentado para valorar la flexibilidad:

Capacidad aeróbica: El volumen de oxígeno máximo (VO₂max) se estimó a través del test de campo incremental máximo de ida y vuelta de 20 metros. El test consiste en recorrer dos líneas separadas 20 m siguiendo el ritmo que marca el protocolo. Dicho ritmo comienza determinando una velocidad de carrera de 8,5 km/h y se incrementa 0,5 km/h cada minuto. La prueba finaliza cuando el niño se detiene o no es capaz

de llegar a la línea según la señal sonora por segunda vez consecutiva. Se registró el número de minutos (enteros o medios) que el alumno completó. A partir de ese dato, calculamos el VO₂max en relación a la masa corporal (ml/kg/min) mediante las fórmulas establecidas por Léger²⁴. En función del VO₂max y según los últimos estándares de referencia Fitnessgram para cada edad y sexo²⁵, se clasificó a los alumnos en “zona saludable”, “algún riesgo” y “alto riesgo”. No obstante, debido al bajo número de escolares en el grupo de “alto riesgo” (menos de un 5%), se agruparon las dos últimas categorías.

Fuerza muscular:

a) **Test de dinamometría manual.** Esta prueba evalúa la fuerza máxima isométrica de prensión manual a través de un dinamómetro digital (TKK5101, Tokio, Japón; rango 5 a 100 kg, precisión 0,1 kg). El test consiste en aplicar la máxima prensión manual en una posición estandarizada, de pie, con los brazos paralelos al cuerpo, y sin contacto con el dinamómetro, excepto la mano que es evaluada. Se graduó el agarre del dinamómetro al tamaño de la mano de cada participante²⁶ y se registró la media en kilogramos (kg) de la mejor medida de cada mano.

b) **Test de salto horizontal sin impulso.** Esta prueba evalúa la fuerza explosiva del tren inferior mediante la máxima distancia alcanzada en dos intentos. Se registraron los centímetros (cm) desde el talón más atrasado hasta la línea de despegue.

Capacidad motora: La velocidad-agilidad se valoró mediante el test 4 x 10 m. Consiste en recorrer un espacio de 10 metros en cuatro ocasiones, en el menor tiempo posible y recogiendo del suelo tres esponjas (una cada 10 metros recorridos), situadas tras las líneas que determinan dicha distancia. Se registraron los segundos (s) y décimas de segundo en completar el recorrido.

Flexibilidad: flexión de tronco en posición de sentado. Este test evalúa la flexibilidad de la musculatura isquiotibial y lumbar del alumno. Partiendo de la posición de sentado en el suelo con las piernas completamente estiradas y descalzo, consiste en flexionar el tronco todo lo posible hacia delante, sin doblar las piernas y mediante un movimiento continuo y sostenido. Se registraron los centímetros (cm) que sobrepasaron las puntas de los pies con las dos manos paralelas.

Todos los test se realizaron dos veces, registrando la mejor marca, excepto la prueba de capacidad aeróbica que se desarrolló una sola vez.

Diseño de la recopilación de datos

La investigación se llevó a cabo durante los meses de febrero y marzo de 2012. Durante dichos meses, se visitaron las 31 escuelas de la ciudad a razón de una por

día laboral. La recopilación de datos siempre se llevó a cabo entre las 9:00 y las 12:30 horas de la mañana, por el mismo equipo de investigadores y siguiendo el siguiente protocolo de actuación: cumplimentación de los cuestionarios, tensión arterial, antropometría y maduración sexual, y test de condición física. Previo acuerdo con los centros escolares, las pruebas de aptitud física se desarrollaron en el polideportivo y el resto de valoraciones en un espacio habilitado a tal fin por los propios centros.

Análisis estadístico

Las variables cuantitativas se presentan con la media y la desviación típica. La normalidad de los datos se comprobó mediante el test de Kolmogorov-Smirnov. Las comparaciones de las variables con distribución normales se realizaron mediante la prueba T de Student (comparación entre dos grupos) o ANOVA de medidas repetidas de un factor (para comparación de más de dos grupos). Aquellas variables con distribución no normal fueron analizadas mediante las pruebas U de Mann-Whitney y Kruskal Wallis, respectivamente. A través del test Chi-cuadrado de Pearson se analizó la asociación de las variables cualitativas, que se presentan según su distribución de frecuencias.

Se clasificó el rendimiento en cada una de las pruebas de condición física en cuartiles para cada uno de los sexos, estimando el riesgo de padecer sobrepeso u obesidad según los diferentes cuartiles de cada prueba mediante un modelo de regresión logística simple. Se estudió la asociación entre las variables de condición física con las variables antropométricas y la tensión arterial mediante la correlación de Pearson o Spearman, en función de su distribución. También se analizaron las correlaciones parciales controlando los efectos de la variable sexo. Por último, se realizó un modelo de regresión lineal simple entre el VO2max y el porcentaje de grasa.

Los datos fueron analizados con el programa estadístico IBM SPSS versión 20,0 para Windows. El nivel de significación se estableció en 0,05.

Resultados

La edad, desarrollo madurativo, tensión arterial, características antropométricas y nivel de condición física de la muestra de estudio se recogen en la tabla I. Los grupos se dividieron en función del sexo, el tipo de centro, la nacionalidad de origen (español o extranjero) y la presencia o no de sobrepeso u obesidad. Según el tipo de centro, no se encontraron diferencias significativas en ningún parámetro a excepción de la edad, superior en los alumnos de la escuela pública ($p < 0,05$). Lo mismo ocurrió al estudiar a los escolares por su nacionalidad, siendo mayores los alumnos inmigrantes, tanto en su edad cronológica como en los dos indicadores de desarrollo biológico ($p < 0,01$).

En función del sexo, las niñas mostraron un estado madurativo superior al de los niños y unos valores mayores de porcentaje graso, mientras que los niños registraron un mayor perímetro de cintura, siendo estas diferencias estadísticamente significativas ($p < 0,05$). En relación a la condición física, los niños obtuvieron rendimientos superiores de VO2max, fuerza explosiva del tren inferior y velocidad, mientras que las niñas obtuvieron puntuaciones superiores en la prueba de flexibilidad ($p < 0,01$ en todos ellos).

Según el IMC, la prevalencia de sobrepeso y obesidad de los escolares fue del 23,7% y del 3,3%, respectivamente (25,5% y 0% en niñas; y 22% y 6,5% en niños). La clasificación en “normopesos” y “con sobrepeso u obesidad” reveló diferencias significativas en la tensión arterial y en todas las variables antropométricas, con valores más altos en el segundo grupo ($p < 0,01$). Además, éstos obtuvieron rendimientos inferiores en VO2max, fuerza explosiva del tren inferior y velocidad ($p < 0,001$). Por el contrario, consiguieron mayores puntuaciones en el test de fuerza de prensión manual ($p < 0,001$). No se encontraron diferencias significativas en relación al nivel socioeconómico ni sociocultural de los alumnos.

La tabla II muestra el riesgo de padecer sobrepeso u obesidad en relación con el rendimiento en las diferentes pruebas de valoración de la condición física, el cual se estableció en cuartiles. Se puede observar que a medida que aumentó el rendimiento en las pruebas de fuerza explosiva del tren inferior, velocidad y VO2max, disminuyeron las probabilidades de padecer sobrepeso u obesidad (OR = 0,25 para fuerza explosiva, OR = 0,28 para velocidad y OR = 0,09 para VO2max), al contrario de lo que ocurrió en la prueba de prensión manual. Estas tendencias son más acusadas en el caso de los niños.

Las correlaciones entre las pruebas de condición física, la tensión arterial y las variables antropométricas se pueden observar en la tabla III. Para el total de la muestra, menores valores en las variables antropométricas, especialmente en lo referente al porcentaje graso, se asociaron con mejores rendimientos en las pruebas de velocidad ($r = 0,385$), fuerza explosiva del tren inferior ($r = -0,400$), y VO2max ($r = -0,524$), al contrario de lo que sucedió con la fuerza de prensión manual ($r = 0,259$). Estas asociaciones entre aptitud física y composición corporal fueron más fuertes en el caso de los niños. Los rendimientos entre las cinco pruebas de condición física se asociaron entre sí, especialmente en el caso de las niñas, excepto entre el VO2max y la fuerza de prensión. Únicamente la fuerza de prensión manual mostró relaciones directas con la tensión arterial.

Por último, basándonos en los estándares Fitnessgram²⁵ para la capacidad aeróbica, la tabla IV recoge la distribución de los alumnos en “zona saludable” o “algún/alto riesgo”, en función del sexo, la nacionalidad y la composición corporal. Cabe destacar que el 80% de las niñas y el 88% de los niños se encontraban en la zona

Tabla I
Características de la muestra

	Total (n = 329)	Sexo		Nacionalidad			Tipo de centro			Índice de masa corporal			
		Niñas (n = 161)	Niños (n = 168)	p valor	Español (n = 272)	Extranjero (n = 57)	p valor	Privado (n = 150)	Público (n = 179)	p valor	Normo (n = 240)	Sob/Obe (n = 89)	p valor
Edad (años)	11,7±0,4	11,8±0,4	11,7±0,4	0,348	11,7±0,3	12,0±0,5	0,000***	11,7±0,4	11,8±0,4	0,031*	11,8±0,4	11,7±0,4	0,094
TANNER (estadio)	2,3±0,6	2,5±0,7	2,2±0,5	0,001**	2,3±0,6	2,7±0,7	0,000***	2,3±0,7	2,4±0,6	0,109	2,3±0,6	2,4±0,6	0,216
EPC (años)	-2,5±0,4	-2,4±0,4	-2,6±0,4	0,001**	-2,5±0,4	-2,3±0,5	0,002**	-2,5±0,4	-2,5±0,4	0,297	-2,5±0,4	-2,5±0,4	0,946
PAS (mmHG)	100,8±10,8	100,3±11,1	101,3±10,6	0,275	100,8±10,8	101,0±11,0	0,805	99,7±10,2	101,7±11,3	0,147	98,7±9,8	106,4±11,6	0,000***
PAD (mmHG)	54,3±6,3	53,8±6,1	54,8±6,4	0,150	54,4±6,3	54,1±6,2	0,843	54,2±6,2	54,4±6,3	0,948	53,3±6,1	57,2±5,8	0,000***
Peso (kg)	44,1±9,1	44,0±7,9	44,1±10,2	0,578	44,0±9,0	44,5±9,7	0,485	43,5±8,6	44,5±9,6	0,347	40,3±6,4	54,1±7,8	0,000***
Talla (cm)	149,6±7,0	149,9±6,9	149,2±7,2	0,384	149,3±6,7	151,0±8,3	0,038*	149,4±7,2	149,7±6,9	0,730	148,9±7,0	151,4±6,7	0,003**
IMC (kg/m²)	19,6±3,1	19,5±2,7	19,7±3,4	0,775	19,6±3,1	19,3±3,0	0,674	19,4±2,8	19,7±3,3	0,562	18,1±1,8	23,5±2,3	0,000***
P. cin (cm)	65,6±7,0	64,2±6,1	67,0±7,5	0,001**	65,5±7,0	65,9±7,2	0,612	65,2±6,6	65,9±7,3	0,433	62,6±4,4	73,8±6,0	0,000***
Cin/Cad	0,784±0,05	0,761±0,04	0,805±0,03	0,000***	0,784±0,04	0,786±0,05	0,700	0,783±0,05	0,785±0,05	0,617	0,778±0,04	0,801±0,04	0,000***
% Graso	24,5±9,8	25,1±7,6	23,9±11,5	0,011*	24,8±9,9	23,1±9,2	0,284	23,9±9,2	25,0±10,3	0,393	20,2±6,2	36,0±8,2	0,000***
VO2max (ml/kg/min)	44,8±4,8	43±3,6	46,6±5,2	0,000***	45±4,7	43,8±5,4	0,054	45,2±5	44,5±4,6	0,165	45,7±4,9	42,4±3,7	0,000***
DINA (kg)	20,1±3,8	20,1±3,8	20±3,7	0,747	20±3,7	20,7±4	0,143	20,1±3,7	20,1±3,8	0,961	19,4±3,5	22±3,7	0,000***
4X10 (s)	12,7±0,9	12,9±0,8	12,5±0,9	0,000***	12,7±0,9	12,8±0,9	0,790	12,7±0,9	12,8±0,9	0,427	12,6±0,9	13±0,9	0,000***
Salto (cm)	146±18,9	143±18,9	149±18,5	0,001**	147±18,6	144±20,5	0,245	147±18,7	146±19,1	0,989	149±18,7	139±17,5	0,000***
Flex (cm)	1,3±7,6	4,2±8	-1,6±6,1	0,000***	0,9±7,6	2,8±7,6	0,077	1,7±8,3	0,9±7,1	0,338	1,1±7,5	1,8±8	0,424

*p<0,05; **p<0,01; ***p<0,001.

EPC: Edad al pico de crecimiento; PAS: Tensión arterial sistólica; PAD: Tensión arterial diastólica; IMC: Índice de masa corporal; P. cin: Perímetro de cintura; P. cad: Perímetro de cadera; Cin/cad: Cociente cintura/cadera; VO2max: Volumen máximo de oxígeno; DINA: Fuerza de prensión manual; Flex: Flexibilidad.

Tabla II
Riesgo de padecer sobrepeso(obesidad en función de la condición física (cuartiles)

Test	Cuartil	Total			Niñas			Niños		
		N	OR	95% IC	N	OR	95% IC	N	OR	95% IC
VO2max	Q1: Muy bajo	81	1		40	1		41	1	
	Q2: Bajo	83	0,44	0,23-0,83	42	0,37	0,14-0,97	41	0,50	0,21-1,21
	Q3: Alto	80	0,36	0,18-0,70	39	0,41	0,15-1,08	41	0,32	0,13-0,80
	Q4: Muy alto	81	0,09	0,03-0,22	40	0,24	0,08-0,70	41	0,00	0,00-,
		p-valor global = 0,000			p-valor global = 0,038			p-valor global = 0,104		
Dinamometría manual	Q1: Muy bajo	81	1		40	1		41	1	
	Q2: Bajo	85	2,0	0,84-4,80	41	0,97	0,31-3,07	44	5,74	1,17-28,02
	Q3: Alto	80	4,1	1,80-9,40	40	1,79	0,61-5,22	40	13,00	2,74-61,58
	Q4: Muy alto	81	6,4	2,80-14,50	40	3,14	1,12-8,82	41	18,57	3,95-87,27
		p-valor global = 0,000			p-valor global = 0,069			p-valor global = 0,001		
Salto horizontal	Q1: Muy bajo	82	1		40	1		42	1	
	Q2: Bajo	85	0,90	0,48-1,68	43	0,65	0,26-1,63	42	1,22	0,51-2,89
	Q3: Alto	80	0,36	0,18-0,74	38	0,38	0,13-1,07	42	0,35	0,13-0,93
	Q4: Muy alto	80	0,25	0,12-0,54	40	0,35	0,13-1,00	40	0,16	0,05-0,54
		p-valor global = 0,000			p-valor global = 0,148			p-valor global = 0,002		
4 x 10	Q1: Muy bajo	77	1		37	1		40	1	
	Q2: Bajo	76	0,82	0,43-1,57	43	1,01	0,39-2,57	33	0,72	0,28-1,83
	Q3: Alto	84	0,38	0,19-0,76	37	0,58	0,20-1,63	47	0,26	0,10-0,68
	Q4: Muy alto	89	0,28	0,13-0,58	44	0,39	0,14-1,14	45	0,20	0,07-0,56
		p-valor global = 0,001			p-valor global = 0,225			p-valor global = 0,003		
Flexión de tronco	Q1: Muy bajo	89	1		41	1		48	1	
	Q2: Bajo	79	0,79	0,38-1,61	40	0,75	0,25-2,27	39	0,84	0,32-2,17
	Q3: Alto	88	1,41	0,74-2,70	42	2,19	0,83-5,75	46	0,96	0,39-2,34
	Q4: Muy alto	71	1,13	0,56-2,27	38	1,10	0,39-3,16	33	1,21	0,47-3,15
		p-valor global = 0,416			p-valor global = 0,169			p-valor global = 0,913		

Tabla III
Coeficientes de correlación entre la condición física y la tensión arterial y medidas antropométricas

	PAS	PAD	Peso	IMC	P. Cin	% Graso	VO2	DINA	Salto	4 x 10	Flex
VO2max	0,060	-0,105	-0,192*	-0,258**	-0,264**	-0,391**	1,000	0,107	0,460**	-0,517**	0,183*
DINA	0,318**	0,143	0,658**	0,448**	0,438**	0,121	0,107	1,000	0,199*	-0,252**	0,177*
Salto	-0,125	-0,160*	-0,165*	-0,235**	-0,295**	-0,373**	0,460**	0,199*	1,000	-0,677**	0,304**
4 x 10	-0,010	0,090	0,062	0,118	0,250**	0,347**	-0,517**	-0,252**	-0,677**	1,000	-0,335**
Flex	0,006	0,045	-0,009	0,037	-0,065	-0,119	0,183*	0,177*	0,304**	-0,335**	1,000
VO2max	-0,058	-0,064	-0,416**	-0,462**	-0,459**	-0,548**	1,000	-0,103	0,520**	-0,639**	-0,009
DINA	0,427**	0,231**	0,675**	0,535**	0,573**	0,355**	-0,103	1,000	0,090	0,007	0,112
Salto	0,018	-0,083	-0,241**	-0,295**	-0,304**	-0,386**	0,520**	0,090	1,000	-0,646**	0,210**
4 x 10	0,000	0,061	0,311**	0,301**	0,328**	0,403**	-0,639**	0,007	-0,646**	1,000	-0,133
Flex	0,024	0,040	0,009	0,055	0,010	0,005	-0,009	0,112	0,210**	-0,133	1,000
VO2max	-0,017	-0,085	-0,377**	-0,417**	-0,428**	-0,524**	1,000	-0,017	0,508**	-0,607**	0,114*
DINA	0,384**	0,215**	0,654**	0,489**	0,494**	0,259**	-0,017	1,000	0,172**	-0,147**	0,174**
Salto	-0,059	-0,152**	-0,230**	-0,276**	-0,308**	-0,400**	0,508**	0,172**	1,000	-0,714**	0,250**
4 x 10	-0,009	0,105	0,204**	0,221**	0,273**	0,385**	-0,607**	-0,147**	-0,714**	1,000	-0,240**
Flex	0,024	0,034	0,003	0,059	-0,014	-0,058	0,114*	0,174**	0,250**	-0,240**	1,000

*p<0,05, **p<0,01.

*Análisis controlando el efecto del sexo.

VO2max: Volumen máximo de oxígeno; DINA: Fuerza de prensión manual; Flex: Flexibilidad; PAS: Tensión arterial sistólica; PAD: Tensión arterial diastólica; IMC: Índice de masa corporal; P.Cin: Perímetro de cintura.

Tabla IV
Prevalencias de alumnos clasificados como “saludables” y “con algún/alto riesgo” en función de diferentes factores

		Sexo		Nacionalidad		Índice de masa corporal	
		Niñas	Niños	Español	Extranjero	Normo	Sob/Obe
Saludables	N	129	145	234	40	213	61
	%	80,1	88,4	86,7	72,7	90,3	68,5
Con algún o alto riesgo	N	32	19	36	15	23	28
	%	19,9	11,6	13,3	27,3	9,7	31,5
		p = 0,040		p = 0,010		p = 0,000	

saludable, presentando éstos más opciones de encontrarse en la misma (OR = 1,89). De manera inversa, los nacidos fuera de España, así como los que padecían sobrepeso u obesidad, tenían menos probabilidades de tener valores saludables que sus pares españoles (OR = 0,41) y normopesos (OR = 0,24), respectivamente.

Discusión

Los resultados del estudio indicaron que los niños poseen un mayor nivel de condición física con respecto a las niñas, lo cual ya se había constatado anteriormente en pruebas de salto, velocidad y capacidad aeróbica²⁷. Sin embargo, no se encontraron diferencias significativas en cuanto a la fuerza de prensión manual, al contrario de lo que se había confirmado en escolares ingleses²⁸, donde los niños reportaron valores superiores para la edad estudiada (19,6 kg los niños y 18,7 kg las niñas). En ambos casos, los resultados obtenidos fueron inferiores a los de este estudio. A pesar del constatado descenso en la capacidad aeróbica de los niños en los últimos años²⁹, el 88% de los alumnos y el 80% de las alumnas mostraron unos niveles saludables. Estos porcentajes son similares a los encontrados anteriormente en adolescentes españoles, con un 80,7% de los chicos y un 82,7% de las chicas alcanzando dichos niveles³⁰, pero superiores a los de chicos (61%) y chicas (53%) de 10 a 18 años portugueses³¹.

También encontramos diferencias en cuanto a la capacidad aeróbica entre alumnos nacidos en España y nacidos en otros países. Éstas no se aprecian al estudiar los valores absolutos de VO2max de cada uno de estos grupos, lo que pudiera deberse a que la fórmula de Léger disminuye, en este caso, dichas diferencias, ya que tiene en cuenta la edad cronológica, mayor en los inmigrantes. De cualquier modo, una vez clasificados los alumnos en función de su edad y sexo, observamos que las probabilidades de los nacidos fuera de España de alcanzar valores saludables son inferiores (OR = 0,41) a las de los españoles. Este hecho podría estar relacionado con la menor cantidad de práctica física reportada por niños inmigrantes alemanes, condición que explicó el 1% de la varianza de su actividad física³², o con la menor participación (OR = 0,31) de los mismos en actividades deportivas³³. Con respecto a la

situación económica, estudios previos encontraron asociaciones positivas entre escolares que vivían en condados de altos ingresos y su condición física, principalmente, en lo referente a la capacidad aeróbica³⁴. Sin embargo, en nuestros resultados, el nivel socioeconómico no fue un factor determinante.

Según el IMC, los alumnos normopesos lograron mejores rendimientos en velocidad, fuerza explosiva del tren inferior y VO2max, mientras que quienes padecían sobrepeso u obesidad obtuvieron valores superiores en la fuerza de prensión manual, lo cual pudiera deberse a una mayor masa magra. Estos resultados coinciden con otros publicados con anterioridad³⁵ y confirman, tanto en niños como en niñas, la relación entre las posibilidades de padecer sobrepeso u obesidad y un peor rendimiento en pruebas que requieren el desplazamiento de la masa corporal, como es el caso de la velocidad, la fuerza explosiva del tren inferior y, especialmente, el VO2max.

Los resultados del estudio revelaron relaciones significativas, más consistentes en el caso de los niños, entre el rendimiento en las pruebas de fuerza explosiva del tren inferior y velocidad, y las variables antropométricas, al igual que se había constatado anteriormente en escolares canadienses de 10 años³⁶. En concreto, dichos chicos registraron relaciones entre la prueba de salto y el IMC de $r = -0,40$ y las chicas de $r = -0,32$, mientras que las relaciones con la prueba de velocidad fueron de $r = -0,36$ y $r = -0,25$, respectivamente. Los valores para la asociación con el perímetro de cintura fueron muy similares.

No obstante, los mayores coeficientes de correlación se dieron con la capacidad aeróbica. Relaciones con el perímetro de cintura ($r = -0,20$) en niños y adolescentes europeos⁵, con el IMC ($r = -0,73$) en niños chinos⁶ y con ambos en adolescentes españoles³⁷, ya se habían reportado anteriormente. En cualquier caso, las asociaciones más fuertes en ambos sexos se establecieron de manera inversa entre el VO2max y el porcentaje de grasa, llegando a explicar el primero el 18% de la variabilidad del porcentaje de grasa corporal en las niñas y el 32% en los niños. Esta relación, aunque con valores inferiores ($r = -0,45$ en niños y $r = -0,33$ en niñas), también había sido descrita anteriormente³¹.

En lo referente a la tensión arterial, los resultados no mostraron relación entre la capacidad aeróbica y la presión arterial sistólica, aunque sí una débil asociación

con la diastólica, lo que se había documentado anteriormente en el caso de las niñas³⁸. Sin embargo, aunque en todos los casos eran significativas, las relaciones entre las variables antropométricas y la tensión arterial se atenuaban en los alumnos con valores saludables de VO₂max, lo que podría ser indicador de un efecto protector de la capacidad aeróbica sobre la tensión arterial, tal como se constató en niños europeos³⁹.

En cuanto a la asociación entre el rendimiento de las diferentes pruebas de condición física, nuestros resultados revelaron relaciones, tanto en niños como en niñas, entre la capacidad aeróbica y los valores del resto de capacidades evaluadas, excepto con la fuerza de prensión manual. Estos mismos resultados ya se habían encontrado en adolescentes españoles³⁰.

Limitaciones

Nuestro estudio contó con una serie de limitaciones. Principalmente, en referencia a la composición corporal, los pliegues cutáneos no nos aportan información sobre la masa magra o sobre la distribución de la grasa corporal. De igual modo, la realización de test de campo para estimar la capacidad aeróbica no es tan exacta como las pruebas de laboratorio. En cualquier caso, tanto la toma de pliegues como los test utilizados han demostrado una alta validez y fiabilidad, por lo que fueron adecuados para el trabajo de recolección de datos llevado a cabo en las escuelas. Por otro lado, el carácter transversal del estudio hace que no se puedan obtener relaciones de causalidad en las asociaciones entre la condición física y la composición corporal, por lo que más estudios longitudinales y de intervención son requeridos en este sentido.

Conclusiones

Los escolares de género masculino y los normopesos reportaron rendimientos superiores en las pruebas de condición física que las chicas y que quienes padecían sobrepeso u obesidad, respectivamente. Asimismo, en relación al VO₂max, las niñas y los inmigrantes presentaron menos probabilidades de poseer niveles saludables de capacidad aeróbica que los niños y que sus pares nacidos en España.

Las relaciones que se encontraron entre la condición física y la composición corporal ponen de manifiesto la importancia de realizar intervenciones destinadas a mejorar la condición física de los más jóvenes, especialmente su capacidad aeróbica, con el fin de lograr una composición corporal más saludable. Además, dichas intervenciones deberían hacer hincapié en los alumnos inmigrantes y de género femenino.

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Original / Deporte y ejercicio

Unusual antibiotic presence in gym trained subjects with food intolerance; a case report

Alessandro Di Cerbo¹, Sergio Canello², Gianandrea Guidetti³, Carmen Laurino⁴ and Beniamino Palmieri⁴

¹Poliambulatorio del Secondo Parere. Department of Consultation and Coordination. Viale Reiter 14. 41225 Modena. Italy.

²Via Euganea villa 1 - villa di teolo. 35037 Padova. Italy. ³Via Alfonso Chierici 1. 42121 Reggio Emilia. Italy. ⁴Azienda Ospedaliero-Universitaria Policlinico di Modena. Surgery and Surgical Specialties department. University of Modena and Reggio Emilia. Via del Pozzo 71. 41124 Modena. Italy.

Abstract

Introduction: Great interest is raising in food intolerances due to the lack, in many cases, of a particular sensitizing agent.

Objective: We investigated the serum level of possible new haptens in 15 heavy meat consumers for sport fitness affected by various kinds of food intolerance and who had ever been administered antibiotics in their life for clinical problems.

Methods: Forty ml of blood were drawn from each patient and analyzed, by means of an ELISA test, in order to possibly identify the presence of an undue contaminant with hapten properties.

Results: Four out of fifteen subjects (26%) showed a serum oxytetracycline amount > 6 ng/g (which is considered the safety limit), 10 of 15 (66%) a serum doxycycline amount > of 6 ng/g and 3 out of 15 (30%) subjects had high serum level of both molecules.

Conclusions: Although a direct ratio between body antibiotics remnant storage in the long run and chronic gut dysfunctions and/or food allergy did not reached the evidence yet, the blood traces of these compounds in a food intolerant otherwise healthy population might be considered the preliminary putative step of a sensitizing pathway. Our next goals foresee a deeper insight into the sensitizing trigger from human chronic antibiotic exposure via the zootechnical delivery of poultry food.

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Key words: Poultry. Oxytetracycline. Doxycycline. Food intolerances.

PRESENCIA DE ANTIBIÓTICOS INUSUAL EN EL GIMNASIO ENTRENADO SUJETOS CON INTOLERANCIA A LOS ALIMENTOS; INFORME DE UN CASO; ESTUDIO PRELIMINAR

Resumen

Introducción: La falta, en muchos casos, de un agente sensibilizador está despertando un enorme interés en la tolerancia a los alimentos.

Objetivo: Investigamos el nivel sérico de posibles nuevos haptenos en 15 grandes consumidores de carne para entrenamiento deportivo afectados por diversos tipos de intolerancia a los alimentos y que habían recibido antibióticos en algún momento de sus vidas por problemas médicos.

Métodos: Se realizaron extracciones de sangre de 40ml a cada paciente y se analizaron empleando un test ELISA, para identificar la posible presencia de un elemento contaminante indebido con propiedades de hapteno.

Resultados: 4 de 15 sujetos (26%) mostraron una cantidad de oxitetraciclina en suero > 6 ng/g (considerado el límite de seguridad); 10 de 15 (66%) sujetos presentaron una cantidad de doxiciclina > 6 ng/g; y 3 de 15 (30%) sujetos presentaron un alto nivel sérico de ambas moléculas.

Conclusiones: Aunque no se llegó a obtener evidencia de una relación directa entre la acumulación de antibióticos corporales a largo plazo y una disfunción intestinal crónica y/o alergias a los alimentos, las trazas en sangre de estos compuestos en una población con alguna intolerancia a los alimentos pero por lo demás sana, podría considerarse el primer paso de una vía de sensibilización. Nuestros próximos objetivos prevén un estudio más profundo del desencadenante sensibilizador a partir de la exposición crónica a antibióticos en humanos por medio de la administración zootécnica de comida avícola.

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Palabras clave: Aves. Oxitetraciclina. Doxiciclina. Intolerancia a los alimentos.

Correspondence: Alesandro Di Cerbo.
Poliambulatorio del Secondo Parere.
Department of Consultation and Coordination.
Viale Reiter, 14.
41125 Modena. Italy.
E-mail: Alessandro811@hotmail.it

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Abbreviations

APC: Antigen-presenting cells.

ELISA: Enzyme-linked immunosorbent assay.

Introduction

Food intolerances and food allergies are two different gut pathology chapters. In fact while the first involve nonimmunologic adverse reactions to food and include conditions such as lactase deficiency, dietary protein-induced enterocolitis syndromes and eosinophilic gastrointestinal disease, the second are considered adverse health effects arising from a specific immune response that occurs on exposure to a given food.^{1,2}

Loss of tolerance to foods leads to induction of type I hypersensitivity reactions which are influenced by several factors including genetic susceptibility, the nature of antigen which initiates the disease and challenge with infections and bacteria.³ Depending on the stimulus naive T cells are activated by professional antigen-presenting cells (APC) and differentiate into Th1, Th2, Th17 or Th9 cells.⁴ Once Th2 response is established, the mechanism of allergic disease is divided in two main phases: first sensitization, and development of memory and later followed by effector phase and tissue injury. In the first phase, which regards IL-4 and IL-13 production by allergen-specific CD4⁺Th2 cells, a B cell class-switch induction into the antibody isotypes of ϵ immunoglobulin heavy chain and allergen-specific IgE antibody production are observed. Subsequently, allergen-specific IgE, binds to high affinity receptor for IgE on the surface membrane of mast cells and basophils leading to the sensitization of the patients to a specific allergen. Once patient is newly exposed to the sensitized allergen the aggregation of receptor-bound IgE molecules occurs and first the activation and then the release of mediator lead to the development of clinical symptoms⁵ of type I hypersensitivity reactions.^{6,7}

In testing for food sensitivity, blood samples are exposed to a panel of both foods and food components and the degree of total immunoglobulin G antibody binding to each food is quantified by means of an enzyme- or fluorescence- linked immunosorbent assay (ELISA).⁸ Another well established test is that based on the IgG subclass 4 (IgG4) binding (measured in lieu of total IgG).⁹ The causes of food allergy can be related both to genetic factors and environmental exposure^{10,11} and prevention policy¹² would significantly reduce the morbidity and the costs of managing this disorder.¹³ Updates on this issue didn't add any effective therapeutic strategy to overwhelm the problem, except the deprivation diet,¹⁴ dietary supplementation with zinc and copper¹⁵ or the pharmacological approach with disodium cromoglycate,¹⁶ steroids, azathioprine and cyclosporin.¹⁵

The hypothesis that heavy and prolonged eating of antibiotic treated poultry might promote somehow the food intolerance seems worth to be investigated.

Methods

We investigated 15 gym trained subjects (10 males and 5 females, mean age $\pm$ SEM 30.4 ± 2.65 years) with clear cut clinical food intolerance symptoms (i.e. itching, nausea, vomiting, eczema, weakness)^{2,17} admitted to our clinic for proper diagnosis and treatment. A history of "healthy" nutrition (i.e. reach in fibers and poor in carbohydrates) was reported as well as an overall exceeding daily intake of white meat ranging from 300 to 600 gr/day. Forty ml of blood were drawn from each patient and analyzed, by means of an enzyme-linked immunosorbent assay (ELISA) test, in order to possibly identify the presence of an undue contaminant with hapten properties.

In table I the antibiotic remnants levels in each patient serum have been summarized.

Results

Results indicate that although oxytetracycline serum levels of 11 out of 15 subjects (73%) are below the safety level (< 6 ng/g), 4 out of 15 (27%) present alarming serum levels of such molecule. Conversely,

Table I
Schematic representation of serum concentrations of two antibiotics (oxytetracycline and doxycycline)

Subject	Oxytetracycline amount (ng/g)	Doxycycline amount (ng/g)
1	1.97	1.26
2	1.73	8.93*
3	2.09	8.68*
4	1.99	6.60*
5	4.53	6.62*
6	8.19*	6.71*
7	7.17*	5.39
8	3.60	1.78
9	3.16	5.71
10	5.56	7.56*
11	3.30	7.40*
12	4.24	7.85*
13	7.24*	9.40*
14	8.32*	7.40*
15	4.51	4.28

*Means a value which is above the safety limit (6 ng/g).

doxycycline serum levels are above the safety allowed level in 10 out of 15 (66%) subjects and below in 5 out of 15 (33%) subjects. Interestingly, high serum levels of both molecules were observed in 3 out of 15 (30%) subjects.

Further, the IgG-mediated foodstuffs intolerance analysis revealed that all the subjects were intolerant to chicken, 14 out of 15 subjects (93%) were also intolerant to pork, soybean, flax seeds, eggs and corn; 13/15 (86%) also to oat; 12/15 (80%) also to yeast and peas; 11/15 (73%) also to rabbit; 10/15 (73%) also to potato; 9/15 (60%) also to rice; 3/15 (20%) also to salmon, turkey and wheat; 2/15 (13%) also to beef and cheese and 1/15 (6,5%) also to lamb, deer and tuna (fig. 1).

Discussion

Our preliminary clinical investigation opens a possible work hypothesis about the causes of multiple food intolerance, based on a possible haptenic toxic sensitizing mechanism due to prolonged subliminal oral intake of meat from animals grown under chronic tetracycline administration regime.

The bioavailability of this antibiotic, administered accordingly to the international health protocols, encloses, in the long run schedule, a final storage in the animals bone, fat and muscles that theoretically might be transferred to the final consumer and, finally, act as hapten-inducing specific intolerance to a wide range of different foods and molecules such as vegetables, fruits, carbohydrates, and proteins.

As matter of fact in our pilot trial group only 26% of subjects showed normal serum levels of both antibiotic molecules, while the remaining 74% had higher concentrations of at least one form of antibiotic molecule in the blood.

Obviously the small sample of recruited cases is inadequate to draw statistical conclusions about the significance of tetracycline contamination in an healthy hyper-nourished athletes population, but we can open the debate about indirect consequences of long term exposure to this antibiotic molecule, whose structure is basically still provided with sensitizing properties (for instance to the sun light and UV- irradiated skin).

Conclusions

Our next study is going back to the *in vitro* human cells model, adding minimal doses of tetracycline in the culture medium, in order to detect the lowest concentration able to induce some biochemical imbalance via oxidative stress activation, or reducing the concentration of energy releasing molecules from mitochondria. This cells biology insight is supposed to be very helpful in supporting the clinical explanation, in terms of gut mucosal disorder and wide food sensitization.

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Declaration of interest statement

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

The authors hereby certify that all work contained in this article is original.

The authors claim full responsibility for the contents of the article.

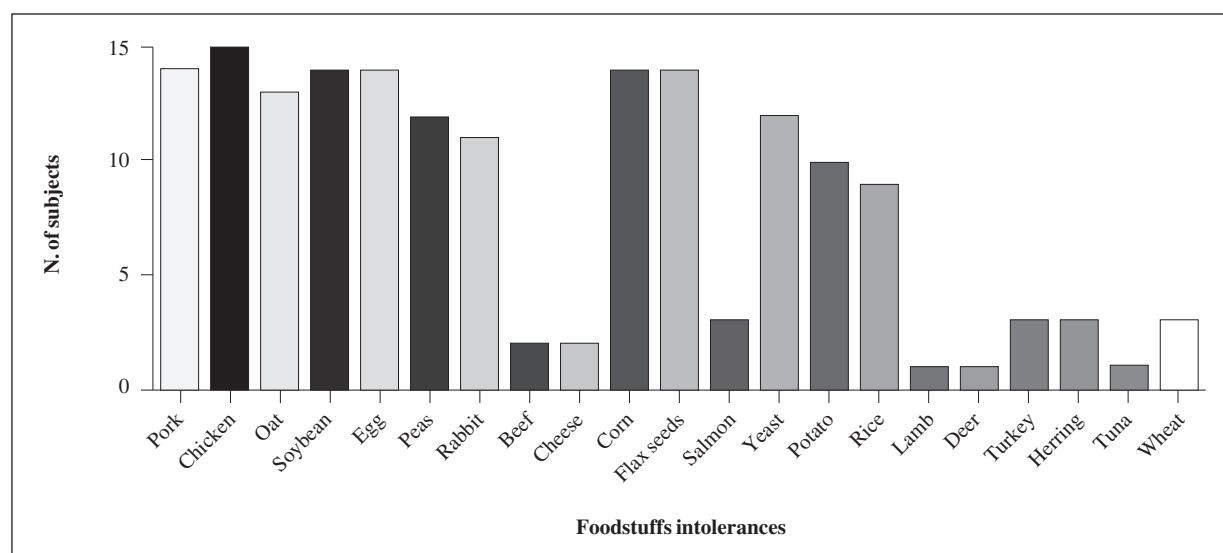


Fig. 1.—Schematic representation of ELISA test of foodstuffs intolerances of gym trained subjects.

Consent

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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Original / Deporte y ejercicio

Swimming training repercussion on metabolic and structural bone development; benefits of the incorporation of whole body vibration or pilometric training; the RENACIMIENTO project

A. Gómez-Bruton^{1,2}, A. Gonzalez-Agüero^{1,3}, J. A. Casajús^{1,2} and Germán Vicente Rodríguez^{1,2}

¹GENUD "Growth, Exercise, NUtrition and Development" Research Group. Universidad de Zaragoza. Spain. ²Faculty of Health and Sport Science (FCSD). Department of Physiatry and Nursing. Universidad de Zaragoza. Huesca. Spain.

³Department of Sports and Exercise Science. Aberystwyth University. UK..

Abstract

Introduction: Enviromental factors such as exercise participation and nutrition have often been linked to bone improvements. However, not all sports have the same effects, being non-osteogenic sports such as swimming defined as negative or neutral sports to practice regarding bone mass by some authors, similarly exercise-diet interaction in especific groups is still not clear.

Objective: To present the methodology of the RENACIMIENTO project that aims to evaluate body composition and more specifically bone mass by several techniques in adolescent swimmers and to observe the effects and perdurability of whole body vibration (WBV) and jumping intervention (JIN) on body composition and fitness on this population and explore posible diet interactions.

Design: Randomized controlled trial.

Methods: 78 swimmers (12-17 y) and 26 sex- and age-matched controls will participate in this study. Dual energy X-ray, peripheral Quantitative Computed Tomography, Quantitative Ultrasound, Bioelectrical Impedance Analysis, and anthropometry measurements will be performed in order to evaluate body composition. Physical activity, nutrition, pubertal development and socio-economical status may act as confounders of body composition and therefore will also be registered. Several fitness factors regarding strength, endurance, performance and others will also be registered to evaluate differences with controls and act as confounders. A 7-month WBV therapy will be performed by 26 swimmers consisting of a training of 15 minutes 3 times per week. An 8 month JIM will also be performed by 26 swimmers 3 times per week. The remaining 26 swimmers will continue their normal swimming training. Four evaluations will be performed, the first one in order to describe differences between swimmers and controls. The second

REPERCUSIÓN DEL ENTRENAMIENTO Y LA PRÁCTICA DE LA NATACIÓN SOBRE EL DESARROLLO METABÓLICO Y ESTRUCTURAL DEL HUESO EN CRECIMIENTO; BENEFICIOS DE LA INCORPORACIÓN DE ENTRENAMIENTO PILOMÉTRICO O VIBRATORIO; EL ESTUDIO RENACIMIENTO

Resumen

Introducción: En la actualidad se ha demostrado que el ejercicio físico y la nutrición mejoran la masa ósea. Sin embargo, existen deportes de bajo impacto como la natación que no presentan efectos positivos en su desarrollo. Además, la interacción ejercicio-dieta y su efecto osteogénico sigue sin estar clara.

Objetivo: Presentar la metodología del proyecto RENACIMIENTO que tiene por objetivo evaluar la composición corporal del nadador adolescente y más concretamente la masa ósea a través de diversas técnicas. Además se pretenden determinar los efectos y la perdurabilidad que pueden tener el entrenamiento vibratorio (WBV) y una intervención con saltos (JIN) sobre la composición corporal y condición física de estos adolescentes, explorando la posible interacción con la dieta.

Diseño: Ensayo clínico aleatorizado.

Metodología: 78 nadadores (12-17 años) y 26 controles del mismo sexo y edad participarán en el estudio. Se utilizarán absorciometría dual de rayos-x, tomografía axial computerizada, ultrasonidos cuantitativo, bioimpedancia eléctrica, y medidas antropométricas para evaluar la composición corporal. La actividad física, nutrición, desarrollo puberal y status socio-económico podrían actuar como covariables de la composición corporal y por lo tanto también serán registradas. Se evaluarán diversos factores de la condición física relacionados con la fuerza, resistencia, rendimiento y otros para definir las diferencias con los controles y para que sirvan como covariables. 26 nadadores realizarán una intervención de WBV 7 meses 15 minutos 3 veces por semana. Además otros 26 nadadores realizarán una JIN 3 veces por semana durante 8 meses. Los 26 nadadores restantes continuarán con su entrenamiento habitual de natación. Se realizaran 4 evaluaciones, la primera de ellas para describir las diferencias existentes entre nadadores y controles, la segunda para describir los efectos de las intervenciones realizadas

Correspondence: Germán Vicente Rodríguez.

GENUD (Growth, Exercise, NUtrition and Development) Research Group. Faculty of Health and Sport Sciences. University of Zaragoza.

Edificio SAI 2ª planta.

Zaragoza. Spain.

E-mail: gervicen@unizar.es

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one to describe the effects of the interventions and the third and fourth evaluations to describe the perdurability of the effects of the WBV and JIN.

Conclusion: The RENACIMIENTO project will allow to answer several questions regarding body composition, fitness, bone mass and interaction with diet of adolescent swimmers, describe swimming as a positive, negative or neutral sport to practice regarding these parameters and elucidate the effects and perdurability of WBV and JIM on body composition.

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Key words: Swimmers. Osteoporosis. Bone mass. pQCT. DXA.

Abbreviations

BIA: Bioelectrical impedance analysis.
BMD: Bone mineral density.
BMC: Bone mineral content.
BUA: Broadband ultrasound attenuation.
CFQ: Calcium frequency questionnaire.
DXA: Dual energy X-ray.
JIN: Jumping intervention.
MICS: Maximum isometric cuadriceps squat.
pQCT: Peripheral quantitative computed tomography.
QUS: Quantitative ultrasound.
RCT: Randomized Controlled Trial.
SOS: Speed of sound.
SES: Socio-economical status.
WBV: Whole body vibration training.

Introduction

It is well known that physical activity has a positive effect on bone mass, and that practiced during growth periods may improve bone acquisition.¹ However, not all sports have the same effects on bone mass. Recent literature suggests that high impact sports such as volleyball or basketball submit bones to higher strains producing increments in bone mineral density (BMD) and bone mineral content (BMC)² and may improve bone structure.³ Other sports like cycling⁴ or swimming that are known as non-impact sports have shown to be less beneficial for bone health than high impact sports being described by some authors as negative sports to practice regarding bone mass.⁵

Focusing on swimming, a recent systematic review⁶ with 52 studies included, concluded that swimmers presented similar BMD and BMC values than sedentary controls, but these results were not conclusive due to the heterogeneity of the included studies. Nevertheless, swimmers presented lower values when they were compared to high-impact sports in all of the studies included in the review. However, the few studies that

y la tercera y cuarta para evaluar la perdurabilidad de estas intervenciones.

Conclusión: El proyecto RENACIMIENTO permitirá contestar a diversas preguntas relacionadas con la composición corporal, condición física y masa ósea de los nadadores adolescentes y el posible efecto combinado dieta-ejercicio en esta población. Definirá la natación como un deporte positivo, neutral o negativo en relación con estos parámetros y esclarecerá los efectos y perdurabilidad de la WBV y JIN sobre la composición corporal.

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Palabras clave: Nadadores. Osteoporosis. Masa ósea. pQCT. DXA.

evaluated bone with peripheral quantitative computed tomography (pQCT) showed that swimmers presented a better structure than sedentary controls. Higher values of bone turnover were also found, suggesting therefore that although swimmers may present similar BMD and BMC values than controls both measured with Dual energy X-ray (DXA), swimmers might present a higher bone quality than sedentary controls.

Most of the studies included in the previous review had reduced sample sizes (n = 20 in most of the studies) to compare with other sports, moreover the authors of the review state that several studies using DXA did not adjust by any covariables and therefore results might have been masking the real effects of swimming. Out of the 52 studies included in the review only 22 included adolescent swimmers and out of these, only 2 included more than 50 swimmers. Moreover, none of the studies including adolescents used pQCT to evaluate bone structure.

Therefore, we propose the following questions:

1. Is swimming negative for bone mass acquisition during adolescence, or does it not have any effect at all in this population?
2. If it is negative, is there a threshold regarding hours of swimming when this activity becomes negative? And regarding years of swimming?
3. If bone structure is analyzed by two methods (pQCT and ultrasound), will there be differences between methods and are swimmers bones stronger, similar or weaker than sedentary controls?
4. Is bone improved with 3 sessions of 15 minutes of whole body vibration training (WBV) or jumping intervention (JIN) complementary to swimming training?
5. If bone is improved with 45 minutes of WBV or JIN per week, what is the perdurability of these effects?
6. Is bone turnover affected by swimming?
7. How does diet interact with exercise and its combined effect on bone mass, structure and metabolism?

These and other questions should be answered, specially in this age-population where bone is constantly developing. The idea that “senile osteoporosis is a paediatric disease” is increasingly accepted.³ In fact, the World Health Organization proposed prevention as the most powerful way to fight against the non-communicable diseases, i.e. osteoporosis.⁷ Adolescence is therefore a critical period for bone development and the effect of intense swimming training on bone should be carefully studied in order to evaluate and avoid bone diseases in this population later in life.

All of the previous questions and the need of describing the art-of-the-state in adolescent swimmers have been the beginning of the RENACIMIENTO project that aims to answer most of these interrogants and elucidate the real effect of swimming on bone mass measured by several different techniques.

With this report we aim to present the general methodology of this wide research project as a way to offer a common comprehensive methodology in this research field.

Material and methods

Arguments for publishing a design paper

The present paper is going to describe a randomized controlled trial (RCT) assessing a WBV and JIN in adolescent swimmers which will take place over a swimming season. Publishing the design and rationale of a RCT before the results are available has important benefits. The study can be critically evaluated for its methodological quality, irrespective of the results. Moreover, if a design paper is written and published, the results will most probably be published, even if they are negative. In addition, a design paper includes a more detailed description of the study techniques, the intervention and all outcome measures than what can be reported in the method section of a regular publication focusing only on part of the study results. This methodological paper can help researchers from similar fields to compare methods and obtain a global view of the project.

Ethical committee

The protocol study has been approved by the Ethics Committee of Clinical Research from the Government of Aragón (C.I.PI11/0034; CEICA; SPAIN), and will follow the ethical guidelines of the Declaration of Helsinki 1961 (revision of Edinburgh 2000), demanding in all cases the signed informed consent by the adolescent participant and his parents or tutors.

Study sample

The RENACIMIENTO study will evaluate 78 adolescent swimmers of both sexes aged from 12 to 17 years old

and 26 adolescent sedentary sex- and age-matched controls not involved in any specific sport participation. All the participants will be healthy adolescents that will not take any drugs affecting bone mass.

The sample size has been calculated in regard to the variable with most variability BMD. An independent t-test was performed in order to attain a power of 99% to detect differences in the contrast of the null hypothesis $H_0: 1 = 2$. Statistical level of significance was set at 1%, and assuming that the mean from the reference group was 1.25 units, the mean of the experimental group 1.20 units and the standard deviation of both groups was 0.02 units it would be necessary to include 10 experimental units in the reference group and 10 in the experimental groups, making a total of 40 experimental units in the study. However, the number of participants to include in a study, also depends of the possible loss of participants: $n' = n/(1-p)$, so if loss were of 30% (possible lost), the number of subjects to recruit would be $n' = 10/(1-0.3) = 12.5$ subjects = 13 subjects in each group. As there are 4 groups (swimmers; swimmers+WBV, swimmers+JIN intervention, controls) and each group is duplicated by sex it makes a total of 104 adolescents (4 groups x 13 participants per group x 2 genders = 104 participants).

Study design

The RENACIMIENTO project is a RCT with follow-up period (fig. 1) where swimmers and controls will be measured in 4 occasions.

The first measurement was performed in September-October 2012. The intervention has been performed, although no results from the first cohort nor the intervention have been published yet.

The second measurement took place in May-June (swimmers) 2013. The effect of WBV, JIN and swimming on bone and body composition during a whole season in adolescent swimmers will be described with this measurement.

The third measurement will take place in February-March, 2014. This measurement will evaluate the perdurability of the effect of the WBV and JIN (if there were any) 9 months after the intervention.

The last measurement will take place in September-October, 2014. With this last measurement we intend to elucidate the perdurability of the effects produced by WBV and JIN on body composition after 18 months.

Equipment

All the used equipment is summarized in table I. Body composition is the main outcome that we intend to measure. However, other factors such as physical activity, nutrition, pubertal development or socio-economical status may act as confounders and therefore must also be recorded.

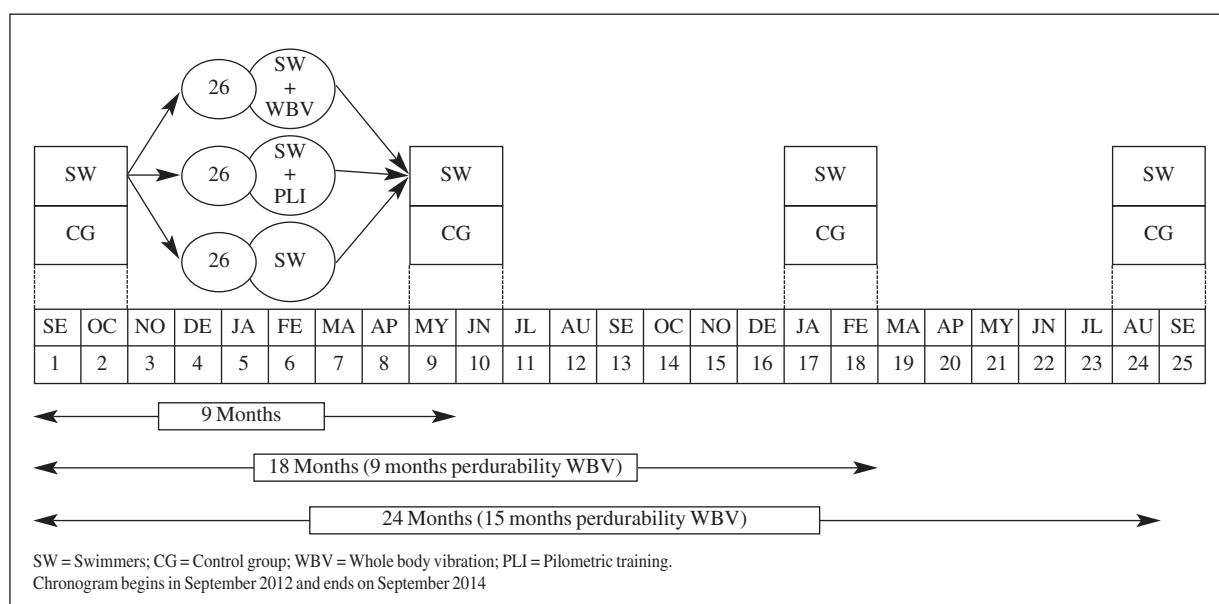


Fig. 1.—Chronological design of the RENACIMIENTO project.

Evaluation

BODY COMPOSITION

One of the main aims of the RENACIMIENTO study is to evaluate bone mass which is the single most important determinant of future fracture.⁸ Several techniques have been designed for this purpose. Included bone mass measurements in this project have been DXA, pQCT and quantitative ultrasound.

DUAL ENERGY X-RAY

DXA is the most common photon absorptiometry method used to evaluate bone mass, and has been defined by the WHO as the gold standard method for evaluating osteoporosis. It is a two dimensional measure highly influenced by body size.⁹ It therefore seems necessary to adjust by covariates to minimize the differences among participants when these are compared. The used equipment for the current project will be an Hologic QDR 4500 scanner (paediatric version of the software QDR-Explorer, Hologic corp., Software version 12.4, Bedford, MA, USA). This device uses two X-ray beams to distinguish between fat and lean tissues on the one hand and bone and soft tissues on the other, on the basis of the extent to which the pairs of tissues attenuate the two X-rays to different degrees. DXA equipment will be calibrated daily using a lumbar spine phantom as recommended by the manufacturer. All DXA scans will be completed with the same device and software and performed by the same technician who has been fully trained in the operation of the scanner, the positioning of subjects, and the analysis of results, according to the manufacturer's

Table I pQCT intra-measures coefficient of variation		
Measure	Zone of evaluation	% coefficient of variation
<i>Radius</i>		
Total area	4%	4.26
Total density	4%	2.25
Trabecular area	4%	4.27
Trabecular density	4%	2.78
Total area	66%	2.42
Total density	66%	2.07
Cortical area	66%	2.44
Cortical density	66%	0.84
Cortical thickness	66%	3.60
Periosteal circumference	66%	1.21
Endosteal circumference	66%	2.98
Muscle area	66%	1.34
Fat area	66%	7.81
<i>Tibia</i>		
Total area	4%	0.82
Total density	4%	0.67
Trabecular area	4%	0.83
Trabecular density	4%	0.90
Total area	38%	4.36
Total density	38%	1.27
Cortical area	38%	5.31
Cortical density	38%	0.49
Cortical thickness	38%	4.61
Periosteal circumference	38%	2.33
Endosteal circumference	38%	2.38
Muscle area	66%	1.69
Fat area	66%	3.88

guidelines. Fat mass, fat-free mass and bone mass are calculated using a computer algorithm provided by the manufacturer. A whole body scan will be performed

allowing a regional analysis (upper and lower extremities and pelvic region). The arm region from the regional analysis includes the hand, forearm and arm and is separated from the trunk by an inclined line crossing the scapulohumeral joint such that the humeral head is located in the arm region. The leg region includes the foot, lower leg and upper leg and is defined by an inclined line passing just below the pelvis crossing the neck of the femur. The head region comprises all skeletal parts of the skull and cervical vertebra above a horizontal line passing just below the jawbone. In addition to this whole body scan a lumbar spine, hip and forearm scans will be performed. To save time and reduce x-ray exposure, only the non-dominant hip and forearm will be scanned. Values for the femoral neck, Ward's triangle, greater trochanter, and intertrochanteric subregions are provided from the hip scan. The Ward's triangle is defined as the area (approximately 1.1 cm²) of the femoral neck with the lowest BMD. Values reported for the lumbar vertebrae L2-L4 are obtained from an anteroposterior lumbar scan and expressed as the mean BMD of the three vertebrae. Values reported for the forearm are ultradistal, mid and 1/3 radius and ulna. The coefficients of variation of the DXA in our lab are published elsewhere.¹⁰

PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY

In contrast to DXA, pQCT measures volumetric BMD and allows for separate assessment of trabecular and cortical bone of the appendicular skeleton, such as the radius and tibia.⁸ This device provides measures of cross-sectional areas related to bone size (area), mass (mineral content), apparent tissue density and geometry (spatial distribution of mass). Moreover, this device calculates strength indices, which combine bone cross-sectional geometry and tissue density measures. Our equipment is a XCT 2000 Peripheral QCT Scanner, Ortometrix, INC that allows measurement of the tibia and radius. For the present study we will use both non-dominant limbs. Coefficients of variation for pQCT in our laboratory have been calculated for several variables and are summarized in table 1. For the calculation of the coefficient of variation the non dominant forearm and lower leg of 20 subjects (16-24 y) were scanned. Two consecutive scans were performed for each limb. All scans and image analysis were performed by the same technician.

QUANTITATIVE ULTRASOUND (QUS)

QUS is a new technology for the assessment of bone strength that measures *speed of sound* (SOS) along the bone and is not affected by bone size, allowing for better comparisons between children of different sizes.¹¹ QUS also provides *broadband ultrasound*

attenuation (BUA) which as SOS, is also related to bone density and structure and to the elastic modulus of bone,¹² but not to cortical thickness.¹³ A Lunar Achilles Insight (Achilles Insight, GE, USA) device will be used to evaluate the calcaneus bone which is the most common measurement site due to its accessibility, suitable shape, and high trabecular content.¹⁴ QUS has been established as an alternative technique for the assessment of bone status,¹⁵ due to the low cost effectiveness and the absence of ionizing radiation. This measurement will be performed in the non-dominant calcaneus.

BIOELECTRICAL IMPEDANCE ANALYSIS (BIA)

BIA is a popular and widely-used method for measuring body composition.¹⁶ This technique determines the electrical impedance of body tissues, which provides an estimate of total body water that is converted to an estimate of fat-free mass, with assumed constant values for the hydration of lean tissue. For our study, a TANITA BC-418 (Tanita, Tokyo, Japan) 8-contact electrode system will be used. Coefficients of variation for BIA in our laboratory have been calculated for weight (0.09%) and body fat percentage (1.11%). For the calculation of the coefficient of variation 15 subjects (16-30 y) were assessed two consecutive occasions.

ANTHROPOMETRY

Researchers were all level 1 or 2 anthropometrists ISAK before the study began. Skinfolts will be measured with a Holtain Harpenden Skinfold Caliper (Holtain, Dyfed, UK) and circumferences with a Rosscraft Anthrotape (Rosscraft Innovations Inc, Vancouver, Canada) (table II). Two researchers will perform anthropometries. To avoid inter-observer error in the longitudinal study, a register will be performed indicating which researcher measured each participant so that the same researcher measures in the different cross-sectional moments of the study the same participant. The technical error of measurement inter and intra-observer will be between the limits recommended by ISAK (< 5% for skinfolts and < 1% for the other measurements).

BONE TURNOVER

Osteoporosis is diagnosed based on an assessment of bone density. However, the results only provide a past history rather than an evaluation of how bone is currently developing. An examination of metabolic markers of bone metabolism can be used to provide an understanding of the dynamic course of bone remodeling. More specifically, serum markers of bone resorption and bone formation can be used to examine the

Table II
Methods included in the RENACIMIENTO project

<i>Outcome</i>	<i>Method</i>	<i>Measurement</i>	<i>Device</i>
Body composition			
	Three-component model	Dual-energy X-ray	Hologic Corp., Software version 12.4, Bedford, MA, USA)
	Two-component model	Bioimpedance	TANITA BC-418 MA
	Skinfold thickness (7 sites)	Subcutaneous fat at defined sites: Biceps, triceps, subscapular, supraspinale, abdominal, front thigh and medial calf	Holtain Harpenden skinfold Caliper
	Circumferences (6 sites)	Arm relaxed, arm flexed and tensed, waist, hip, mid-thigh, calf	Rosscraft Anthrotape
	Quantitative Ultrasound	Calcaneus Speed Of Sound, Broadband Ultrasound Attenuation, and Stiffness Index.	Lunar Achilles Insight
	Peripheral Quantitative Computed Tomography	Bone structure and densities	Stratec XCT 2000 L
	Bone turnover	Osteocalcin, dextrophenylalanine, N-Telopeptides (NTx) and C-telopeptides (CTX)	ELISA Immunoassay
Physical activity			
	Biaxial and triaxial accelerometers	Accelerometry	Actitrainer and Geneactive
	Sedentism questionnaires	Sedentary activities	HELENA screen time-based sedentary behaviour questionnaire ²⁰
Fitness	Physical activity	Practiced sports and hours of physical activity	Self-administered questionnaire
	20 m shuttle run test	Paliers reached in the 20 meter course-navette test	Course navette CD
	Broad-jump	Horizontal distance reached jumping with both feet together	Measuring tape
	30 meter sprint	Time to perform a 30 meter distance	Timing gates (Byomedic fotoelectric cells, Barcelona)
	Maximum isometric strength	Forearm strength	Takey TTK 5401, Tokyo, Japan
		Shoulder strength	SignalframeUSB gauge
		Cuadriceps strength (extensión)	SignalframeUSB gauge
		Cuadriceps strength (squat)	Kistler force plate 9260AA
	Jump evaluation	Squat Jump, Counter Movement Jump, Abalakov	Kistler force plate 9260AA
	Maximum explosive strength	Squat at 20, 30 and 40 % of the maximum isometric quadriceps strength	Kistler force plate 9260AA
Nutrition			
	Helena Dietary Assessment Tool	3 day 24 hour recall	HELENA-DIAT tool
	Calcium frequency questionnaire	Calcium intake	Calcium FFQ (Barr et al.) ²⁶
	Knowledge questionnaire	General nutrition knowledge questionnaire	Self-reported HELENA questionnaire ²⁷
Socio-economical status			
	Socio-economical questionnaire	General socio-economic status	Adapted SES questionnaire ⁴⁶

current and changing status of bone turnover⁽¹⁷⁾. For this purpose, Bone specific Alkaline Phosphatase, and Osteocalcin will be measured in order to evaluate bone formation. For bone breakdown, the measured biomarkers will be N-Telopeptide and C-telopeptide. In addition deoxypyridinoline and N-Telopeptides (NTX) will be determined from immunoassay and ELISA respectively, from a urine sample

PHYSICAL ACTIVITY

ACCELEROMETRY

An Actitrainer accelerometer (ActiTrainer™, Florida, USA) is a small (8.6 x 3.3 x 1.5 cm) and light device. It is

multi-functional composed of heart-rate monitor, solid-state accelerometer, electronic pedometer, inclinometer and an ambient light sensor. The validity and reliability of the Actitrainer-based step counting in non-laboratory conditions has been previously validated⁽¹⁸⁾. Accelerometers will be placed at children's waist at the right side of the body in an elastic belt with a selected epoch length of 15 seconds. Adolescents will be required to wear the accelerometer from the moment they wake up in the morning until bedtime in the evening during 4 consecutive days including a weekend day. However, this accelerometer is not waterproof and therefore will be removed by participants when they have to take a shower or perform aquatic activities.

In the third cross-sectional moment of the study each participant will wear 2 accelerometers. The previously

mentioned actitrainer accelerometer and the GENE. The GENE is a triaxial, ± 6 g seismic acceleration sensor (LIS3LV02DL; STMicroelectronics, Geneva, Switzerland). The small (36 x 30 x 12 mm) and light-weight (16 g) water-proof design of the GENE allows it to be easily worn at multiple locations on the body (e.g., wrist, waist, ankle). The GENE has 500 MB of memory to assist with the storage of the raw 80-Hz sampling frequency and can store ~8 d of data in raw mode with 12-bit resolution. Users have the ability to select user-defined sample frequencies ranging from 10 to 80 Hz. Using the GENE software (version 1.487 update 531), via USB-to-PC connection, 47 GENE accelerometers were initialized to collect unfiltered, triaxial acceleration data at a sampling rate of 80 Hz.¹⁹

SEDENTARISM QUESTIONNAIRE

A sedentary questionnaire including hours of diary television, computer, videogames and several similar sedentary activities will be delivered for the adolescents to complete. This questionnaire has been described elsewhere.²⁰

PRACTICED SPORTS

We will provide a questionnaire asking the current practiced sports, hours per week of practice and years of participation. Past practiced sports that are no longer being practiced will also be questioned in order to have a complete sport history of the participants.

NUTRITION

Nutrition is key to bone mass²¹ and therefore several methods will be used in order to register participants nutritional intake.

HELENA DIETARY ASSESSMENT TOOL

The HELENA-DIAT²² is a computer program that allows participants to register a 24-hour recall. The advantage of using an informatic program is that it allows to view pictures of the food in order to choose the appropriate portion size. A researcher will guide the participants through the program to remind them items that they normally forget such as bread accompanying meals or water. The program calculates the macro- and micronutrients intake of the evaluated day. A total of three 24-hour recalls will be performed (1 of them of a weekend day). The 24-hour recall method has been described as the best method to get population mean intakes and distributions for participants aged 10 and over in different European countries.²³ Moreover, we

have previously used it in our laboratory²⁴ and all researchers are familiar with this tool.

CALCIUM FREQUENCY QUESTIONNAIRE (CFQ)

Several observational studies have suggested that increasing the calcium intake would promote a greater bone mass gain, and thereby a higher peak bone mass.²⁵ This nutrient is an important factor to take into account when studying bone mass. Thus, a specific CFQ elaborate by Barr et al.²⁶ will be used.

NUTRITION KNOWLEDGE

Nutrition knowledge will be assessed by the NKT questionnaire described elsewhere.²⁷

SOCIO-ECONOMICAL STATUS (SES)

It has been shown that SES influences sport participation, nutrition and body composition.²⁸ Therefore, SES is an important confounder that must be taken into account when evaluating these variables and comparing two groups. A questionnaire described elsewhere²⁷ will be used for the evaluation of the SES.

FITNESS

Laboratory and field tests will be performed in order to measure physical fitness and observe the possible relations with body composition, nutrition and socio-economical status.

LABORATORY TESTS

The tests presented below are in the same order as we will perform them in our laboratory.

- *Dynamic strength of the lower limbs.* The generated forces will be measured with a KISTLER platform type 9260AA (Kistler instruments Ltd., Hampshire, UK) while the participants perform 3 different jumps: Squat jump, Countermovement jump and Abalakov jump. The inclusion of the 3 jumps has been decided in order to analyze differences between jumps and evaluate maximal lower limb explosive strength. Participants will perform 3 attempts of each jump with at least one minute rest in between. The best performance will be selected for future statistical analyses.
- *Maximum isometric quadriceps extension strength.* Subjects will be sitting on a table, with an anchorage placed on the distal third of the tibia. This anchorage will be connected to a strain gauge

(MuscleLab, Force Sensor, Norway) that will register the Newtons of isometric force generated during the 6 seconds that participants will have to perform the test. Two attempts will be allowed for each leg, with a minimum of 3 minutes between attempts with the same leg. The best performance will be selected for future statistical analyses.

- *Maximum isometric shoulder flexion strength.* Participants will be encouraged to perform the maximum isometric strength lying on a fitness bench with one arm extended in an overhead position simulating the downstroke phase of freestyle swimming. Participants will perform force against an anchorage connected to a MuscleLab gauge that will register the Newtons of isometric force generated. Two attempts will be performed with each upper limb. The best performance with each upper limb will be selected for future statistical analyses.
- *Maximum isometric cuadriceps squat 90° (MICS).* Participants will be placed in a 90 degree squat position standing on the force platform. They will be encouraged to execute their maximum strength in order to stand up from the 90° squat position, performing strength against a fixed bar that will prevent the subject to move. All the performed strength will be registered by the strength platform and will later be analyzed. The best performance with each leg will be selected for future statistical analyses.
- *Maximum isometric forearm strength.* A digital handgrip dynamometer (Takei TKK 5401, Takei scientific instruments, Tokyo, Japan) will be used in order to evaluate strength of the forearm and hand muscles. Hand span to perform the test will be different for each participant according to their hand size. The dynamometer will be placed according to the optimal handgrip span suggested by Ruiz et al.²⁹ Participants will perform two maximum strength trials with each hand. The best performance with each arm will be selected for future statistical analyses.
- *Muscular power of the lower limbs at 20,30 and 40% of the MICS.* For these tests, participants will start from a standing position. From there, participants will be encouraged to perform a half-squat loading a bar and weight plates added to the bar. With this test it is intended to measure the maximum power that a participant is able to perform during the concentric phase when performing the extension lifting 20, 30 and 40% of their MICS. This will be performed in a machinery in which the resistance bar will be attached at both ends with linear bearing on two vertical bars, thus allowing only vertical movements of the bar. A rotator encoder attached to the bar (Tforce dynamic measurement system, model TF-100, Ergotech consulting S.L. Murcia, Spain) will be used to register the performed power.

FIELD TESTS

- *Standing Broad Jump.* This jump will be performed in order to test explosive leg power. A two-foot take-off and landing will be demanded to the participants, allowing them to swing their arms and bend their knees to provide forward drive. Three attempts will be performed. The best performance will be selected for future statistical analyses.
- *Thirty meters sprint.* The purpose of this test is to determine maximum running speed. Timing gates (Byomedic photoelectric cells, Barcelona) will be placed with 30 meters between them. Participants will start at one gate, and when the researcher gives the start indication, the participant will run as fast as possible to the other gate. This test has shown to have a high predictive value for bone mass and bone mass accumulation during growth.¹⁹
- *Twenty meters shuttle run fitness test.* This test will be performed in order to evaluate $\dot{V}O_{2\max}$ of the participants, using the Leger equation.³⁰ It involves continuous running between two lines 20 meters apart in time to recorded beeps. The speed starts at 8 km/h and increases 0.5 km/h per minute. The test will be stopped if the participant fails to reach the line for two consecutive beeps.

EVALUATION OF PUBERTAL DEVELOPMENT

Pubertal development will be evaluated by self-assessment following the Tanner stages, that has been described as a reliable method for this purpose.³¹

Intervention

Swimmers will be randomly divided into 3 groups. One group will receive an intervention with WBV and another group and intervention based on plyometric training. The third group will consist of swimmers who will continue their habitual training routine and will act as swimming control group.

WHOLE BODY VIBRATION TRAINING

There has been a recent increased interest of WBV.³² This training methodology is considered beneficial for performance³³ and rehabilitation.³⁴ Previous studies suggest that mechanic vibrations applied directly on the muscle fiber, produce reflex muscle contraction due to the tonic vibration reflex.³⁵ Although in non-sportive population it has generally been used in older populations,³⁶ it has also proved its effectiveness improving mobility,³⁷ muscular function³⁸ and bone mass³⁹ in children and adolescents with different pathologies.^{40,41} Recent studies have demonstrated that

Table III
Whole body vibration protocol

<i>Month</i>	<i>Exercises</i>	<i>Total number of exercises</i>	<i>Frequency (Hz)</i>	<i>Amplitude (mm)</i>	<i>Duration (s)</i>	<i>Rest (s)</i>	<i>Total (min)</i>	<i>G-Force</i>
0 (2 weeks)	2 (A,B,C,D,E)	10	30	2	45	45	14.30	2.6
1 (4 weeks)	2 (A,B,C,D,E)	10	30	4	45	45	14.30	5.1
2 (4 weeks)	2 (A,B,C,D,E)	10	32	4	45	45	14.30	5.8
3 (4 weeks)	2 (A,B,C), 1(D,E)	8	34	4	60	60	15	6.6
4 (4 weeks)	2 (A,B,C), 1(D,E)	8	36	4	60	60	15	7.4
5 (4 weeks)	2 (A,B,C), 1(D,E)	8	38	4	60	60	15	8.2
6 (4 weeks)	2 (A,B,C), 1(D,E)	8	40	4	60	60	15	9.1

A = Squat at 120°; B = Squat at 90°; C = Dynamic squat from 90 to 120; D = Lunge right leg; E = Lunge left leg.

WBV performed at low frequencies and amplitudes is safe and effective on the musculo-skeletal system.⁴²

One of the main advantages of WBV is that training sessions can be very short, being 10 minutes enough to produce osteogenic effects. In young women with low BMD, 12 months of WBV (10 minutes, 30HZ, 0.3 g) produced an increase of trabecular bone in the lumbar spine and an increase of the cortical area of the femur bone.⁴³

Adolescent swimmers included in our study are training an average on 10 hours per week, therefore we could not include a type of training that needed of another 2 or 3 extra-hours per week to improve bone mass. The short training times needed for WBV and the benefits on bone mass found in literature, made it our choice to try to improve swimmers bone mass.

WBV DEVICE

The WBV platform used in the study is a Power Plate Pro 5, (PowerPlate, London, UK). The WBV market is extense, the election of this platform was based on the medical certificates supplied by this company and the previous experience of the research group with them.

WBV PROTOCOL

The choosen protocol for the intervention has been designed by an expert of this field that has performed several studies using WBV.^{44,45} The protocol is summarized in table III. The first 2 weeks are an adaptation period, and the intense training begins in week 3 (month 1) and lasts for 6 months.

HIGH IMPACT TRAINING

This programme will consist on a jumping intervention that will take place 3 times per week in 15 minute

sessions. For the design of this intervention easy exercises with accesible material have been choosed. The intervention program is summarized in table IV. A circuit of 4 stations that include high impact jumping (ground reaction forces higher than 3.5 body weight in the lower jumps and over 5 times body weight in the piometric jumps) will be prepared in each sesion, consisting of obstacle jumps with different positions and directions.

The intensity and number of jumps will progressively increase over 4 levels, having each level a duration of 8 weeks. Intensity will be modified increasing the hurdle height from 25 cm in level 1 to 35 in level 4. The volume per sesion will also increase by increasing the jumps from 120 in level 1 to 160 in level 4 with a 1 minute rest between each activity station.

HIGH IMPACT PROTOCOL

Four main exercises will be performed in each session:

- *Hurdle jumping:* Hurdles will be separated by 60-70 cm. Participants will jump 8 consecutive hurdles jumping and landing with both feet simultaneously. Jumps will be performed in a pliometric way, without allowing rest between hurdles. Once they have jumped the 8 hurdles, participants will walk back to the begining to repeat the exercise.
- *One foot bench:* Participants will jump from one side to another of a bench with one foot. Landing each time with a different foot and jumping with that same foot. Once they have ended the bench, participants will walk back to the begining to repeat the exercise.
- *Hurdles back and forward:* Participants will jump a hurdle back and forward jumping and landing with booth feet simultaneously ten times.
- *Two feet bench:* Participants will jump from one side to another of a bench with both feet together. When finished, they will walk back to the begining to repeat the exercise.

Table IV
Jumping high impact intervention

Level	Exercise	Number of series	Number of jumps	Height (cm)	Total jumps	Total session	Total week	Total level
1	Hurdle jumping	3	10	25	30	120	360	2.880
	Bench jump 1 leg	3	10	25	30			
	Hurdle jumping back and forward	3	10	25	30			
	Bench jump 2 feet	3	10	25	30			
2	Hurdle jumping	3	10	25	40	140	420	3.360
	Bench jump 1 leg	3	10	25	40			
	Hurdle jumping back and forward	3	10	25	40			
	Bench jump 2 feet	3	10	25	40			
3	Hurdle jumping	3	10	30	40	160	420	3.840
	Bench jump 1 leg	3	10	30	40			
	Hurdle jumping back and forward	3	10	30	40			
	Bench jump 2 feet	3	10	30	40			
4	Hurdle jumping	3	10	35	40	160	480	3.840
	Bench jump 1 leg	3	10	35	40			
	Hurdle jumping back and forward	3	10	35	40			
	Bench jump 2 feet	3	10	35	40			
Total jumps								13.920

Dissemination plan

Dissemination activities aim to promote international dissemination and exploitation of the RENACIMIENTO results. These results will be presented in national and international congresses and meetings focused on physical activity, swimming and overall sport sciences. Moreover, the likely impact of the results of this research will allow the publication of scientific papers in top journals of the sports science area. In addition to this scientific path, participants will also be informed of the results obtained in the current project. The Spanish Swimming Federation, swimming clubs and Ministry of Education, Culture and Sport will also be informed of the results found by the RENACIMIENTO study.

Perspective

Therefore, the RENACIMIENTO project is aiming to answer as many questions of those proposed in the introduction as possible, in order to better understand the actual effects of intensive swimming training during adolescence on different variables of health, and the possible effects of a WBV and jumping interventions over a season.

These answers will be presented in the form of original research articles, leaded mainly by the three PhD students running the field and laboratory testing during the 3-year project. The different articles, and hence the 3 different PhD theses, will be focused in 3 main areas, previously explained, within the RENACIMIENTO project: 1) body composition, 2) performance and 3) nutrition.

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Original / *Cuidados intensivos*

Anthropometric indicators of nutritional status and growth in very low birth-weight premature infants hospitalized in a neonatal intensive care unit

Edgar M. Vásquez-Garibay^{1,2}, Yonué E. Larios Del Toro², Alfredo Larrosa-Haro² and Rogelio Troyo-Sanromán²

¹Hospital Civil de Guadalajara Dr. Juan I. Menchaca. ²Instituto de Nutrición Humana. Universidad de Guadalajara. México.

Abstract

Background: Anthropometric indicators are difficult to interpret in very low birth weight (VLBW) premature infants, including both appropriate for gestational age (AGA) and small for gestational age (SGA) infants. Therefore, the purpose was to describe the anthropometric indicators of growth and nutritional status in VLBW premature infants AGA and SGA, hospitalized in a neonatal intensive care unit (NICU).

Study design: The descriptive and prospective study design included 114 preterm infants, adequate for gestational age/small for gestational age hospitalized in the intensive care unit. Head, thigh, mid upper arm circumference, skin-fold measurements and weight/age, length/age, and weight/length indices were obtained. Correlations were made among the anthropometric indices, and a multivariate regression analysis with weight/age as dependent variable was performed.

Results: Weight/age in AGA premature infants had high number of significant anthropometric correlations. The SGA premature infants had few and weak correlations. The regression analysis showed that anthropometric indices better explain changes in the weight/age index in adequate for gestational age premature infants.

Conclusion: Weight/age in the VLBW/AGA premature infants could reflect growth, nutritional status and energy stored as fat, but in the VLBW/SGA premature infants, thigh circumference and mid arm circumference would be better indicators just of nutritional status.

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Key words: *Premature infants. Anthropometric indices. Intensive care.*

INDICADORES ANTROPOMÉTRICOS DEL ESTADO NUTRICIO Y CRECIMIENTO EN PREMATURO DE MUY BAJO PESO AL NACER HOSPITALIZADOS EN UNA UNIDAD DE CUIDADOS INTENSIVOS

Resumen

Introducción: Los indicadores antropométricos son difíciles de interpretar en prematuros de muy bajo peso al nacer (MBPN), tanto con peso adecuado para la edad gestacional (PAEG) como peso bajo para la edad gestacional (PBEG). Por tanto, el propósito fue describir los indicadores antropométricos de crecimiento y estado nutricional en prematuros con MBPN con PAEG y PBEG hospitalizados en una unidad de cuidados intensivos neonatales (UCIN).

Métodos: En un estudio descriptivo y prospectivo se incluyeron 114 recién nacidos prematuros, con peso adecuado y bajo para la edad gestacional hospitalizados en la UCIN. Se obtuvieron las mediciones de circunferencia de cabeza, muslo, brazo, pliegues cutáneos y los índices peso/edad, longitud/edad y peso/longitud. Se realizaron correlaciones entre los diferentes indicadores antropométricos y se elaboraron modelos de regresión múltiple con el índice peso/edad como variable dependiente.

Resultados: El índice peso/edad en prematuros con PAEG tuvo el número más elevado de correlaciones significativas. Los prematuros con PBEG tuvieron pocas correlaciones y más débiles. El análisis de regresión múltiple mostró que los indicadores antropométricos explican mejor cambios en el índice peso/edad en prematuros con peso PAEG que en prematuros con PBEG.

Conclusión: El índice peso/edad en prematuros con muy bajo peso al nacer, adecuado para la edad gestacional podría reflejar el crecimiento, el estado nutricional y las reservas de energía. En prematuros con PBEG la circunferencia de muslo y de brazo serían mejores indicadores solo del estado nutricional.

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Palabras clave: *Prematuros. Indicadores antropométricos. Cuidados intensivos.*

Correspondence: Edgar M. Vásquez Garibay.
Instituto de Nutrición Humana.
Hospital Civil de Guadalajara Juan I. Menchaca.
Salvador Quevedo y Zubieta 750.
44340 Guadalajara. Jalisco. México.
E-mail: inhu@cucs.udg.mx

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Introduction

The interpretation of the anthropometric indices of growth and nutritional status differs according to different stages in the pediatric population.¹⁻³ During the first semester of postnatal life, the index weight/age (W/A) would be more useful than the indices length/age (L/A) or weight/length (W/L) for the diagnosis of malnutrition because during the early months of life, the W/A deficit is more pronounced.⁴ Although head circumference (HC) is a natural indicator of brain growth (neurologic development), it is also a good indicator of growth and it is particularly useful during the first semester of postnatal life because it correlates well with L/A even in very low birth weight infants (VLBW).^{1,5}

The mid upper arm circumference (MUAC) has been used for the assessment of nutritional status in children between 6 and 59 months of age.⁶ The skinfold thickness has also demonstrated its reliability in estimating the percentage of subcutaneous body fat.⁷ Some authors⁸ have suggested that in newborn infants, the MUAC and tricipital skin fold (TSF) provide a simple measure of the body composition of neonates and are a useful tool for determining the degree of maturity of a newborn, independent of birth weight, even in premature infants small for gestational age (SGA).⁹ Others (10) have stated that both measurements are inaccurate predictors of the regional body composition in preterm infants, appropriate-for-gestational-age (AGA).

In VLBW premature infants ($\leq 1,500$ g), the use of common anthropometric indices is difficult to interpret, especially in the comparison of premature infants that are AGA or SGA.^{2,3} For these two conditions, the anthropometric diagnosis could have different interpretations because each anthropometric index would acquire a distinct dimension. This different interpretation is particularly true when VLBW premature infants are hospitalized in a neonatal intensive care unit (NICU) and require an integral evaluation of their nutritional status, growth and body composition.^{2,10,11-14} Therefore, the purpose of this study was to describe the anthropometric indicators of nutritional status and growth in VLBW premature infants AGE and SGA that were hospitalized in a NICU.

Subjects and methods

A descriptive study design of two cohorts was used. This study was performed at a tertiary referral center on 114 VLBW preterm infants ($\leq 1,500$ g) of both sexes, with or without underlying pathology¹⁵ who were appropriate or small for their gestational age according to the criteria by Battaglia and Lubchenco.¹⁶ All subjects were hospitalized in the intermediate unit or the NICU at the Civil Hospital of Guadalajara Dr. Juan I. Menchaca from August 2008 to August 2009. The infants with major congenital malformations or those included in any other medical or nutritional protocols

were not included into this study. The protocol of total parenteral nutrition starts on the 2nd day of life. When the patients were stable (no acidosis, normal arterial pressure, respiratory frequency less than 80 per min. and normal intestinal transit), the protocol of enteral feeding was initiated.

Malnutrition was defined as two standard deviations below the mean for one or more of the following indicators: weight for age or MUAC.¹⁷ All subjects were born at the Civil Hospital of Guadalajara Dr. Juan I. Menchaca and were hospitalized in the intermediate and intensive care units. The infants who met the inclusion criteria were included in the study.

After inclusion, 13 cases were excluded because of death soon after the first measurements were made (up to a period of 7 days). From the remaining sample ($n = 101$), nine patients died during the study, twelve were discharged because their health improved and 80 completed the study.

The dependent variables were the following: weight, length, HC, MUAC, thigh circumference (TC), the sum of four skin folds (S 4SF) (tricipital, bicipital, sub scapular and suprailiac); and the W/A, L/A, and W/L indices assessed as the respective z-scores (z). The independent variables were: sex, birth weight, and gestational age; type of feeding and energy intake (kcal/kg/d). Before starting the study, two observers were trained in standardized anthropometric measurements following Habicht's method,¹⁸ and they collected all the anthropometric measurements. The weight was measured with the infant not wearing clothes using a digital pediatric scale (SECA®, Model 364; Tokyo, Japan). The length was measured with an infant measuring board (SECA® Model 416, Tokyo, Japan). The HC, TC and MUAC measurements were taken with a 5 mm wide metallic metric tape (Rosscraft ANTTAPS Anthropometric Tape, USA). The tricipital (TSF), subscapular (SSF), bicipital (BSF) and suprailiac (SISF) skin fold thicknesses were measured using a Lange skin fold caliper (Cambridge, Maryland, USA). All the measurements were obtained using standard procedures.^{19,20} The anthropometric measurements and indices were taken 24 hours after admission and then 7, 15 and 30 days during hospitalization. The criteria for the evaluation of the anthropometric indices of growth were those recommended by the World Health Organization, including the normal limits of ± 2 z scores.¹⁷ The reference standards for W/A, L/A, W/L, HC, and TC were those reported by Usher and McLean.²¹ The reference standards for MUAC were those from Sasanow et al.,²² and the references for the skin folds were those reported by Rodriguez et al.²³

Statistical analysis

For description of the entire cohort, chi square tests were used to compare differences in proportions and for longitudinal analysis of growth outcomes over

Table II
Outcomes of length/age and head circumference for age in AGA and SGA VLBW premature infants during the hospitalization period

Time of measurement (days)	AGA ^a		SGA ^b		p
	Mean	SD	Mean	SD	
Length/age (z)					
Admission	-1.1	1.2	-2.7	0.7	< 0.001
7 th	-1.8	1.1	-2.6	1.0	0.001
14 th	-1.8	1.3	-3.2	0.7	< 0.001
30 th	-2.3	1.3	-3.2	0.9	0.003
HC (z)					
Admission	-1.3	1.1	-2.7	1.0	< 0.001
7 th	-1.8	1.0	-2.2	1.0	0.060
14 th	-1.7	1.1	-2.5	1.1	0.001
30 th	-1.9	1.3	-2.4	1.2	0.080

AGA: Appropriate for gestational age; SGA: Small for gestational age; VLBW: Very low birth weight; X: Mean. SD: Standard deviation; HC: Head circumference.

^aAdmission: n = 57; Day 7: n = 53; Day 14: n = 52; Day 30: n = 49.

^bAdmission: n = 44; Day 7: n = 42; Day 14: n = 42; Day 30: n = 31.

At admission and throughout the entire hospitalization period, the index W/A in the VLBW/AGA premature infants had high number of significant direct correlations, followed by the HC and MUAC. At admission,

the VLBW/SGA premature infants had few and weak correlations, primarily with W/A index. At 14 and 30 days, the index W/A, and the indicator TC showed the majority of significant correlations. Tables III and IV

Table III
Correlation coefficients of anthropometric indicators in AGA/VLBW premature infants. The weight/age z-score was assigned as the dependent variable. All indicators were analyzed as z-scores

Day of measurement	Anthropometrical indicators					
	L/A	W/L	HC	MAC	TC	Σ4SF
Admission (n = 57) ^a	0.745 [†]	0.455 [†]	0.674 [†]	0.540 [†]	0.289*	—
7 th (n = 53) ^b	0.798 [†]	0.295*	0.786 [†]	0.462 [†]	0.649 [†]	0.645*
14 th (n = 52)	0.660 [†]	0.382 [†]	0.719 [†]	0.569**	0.791 [†]	0.388
30 th (n = 49)	0.586 [†]	0.502 [†]	0.682 [†]	0.709 [†]	0.705 [†]	0.641 [†]

AGA: Appropriate for gestational age; VLBW: Very low birth weight; L/A: Length/age; W/L: Weight/length; HC: Cephalic circumference; MAC: Mid arm circumference; TC: Thigh circumference; SF: skin folds.

^aFive premature infants died and three were discharged before the 30th day.

^bΣ4SF n = 14.

*p < 0.05; **p < 0.01; [†]p < 0.001.

Table IV
Correlation coefficients of anthropometric indicators in SGA/VLBW premature infants. The weight/age z-score was assigned as the dependent variable. All indicators were analyzed as z-scores

Day of measurement	Anthropometrical indicators					
	L/A	W/L	HC	MAC	TC	Σ4SF
Admission (n = 44)	-0.064	0.472 [†]	0.184	0.393**	0.341*	0.323
7 th (n = 42) ^a	0.157	0.465**	0.251	0.223	0.616 [†]	0.652 [†]
14 th (n = 42)	0.351*	0.367*	0.640 [†]	0.145	0.692 [†]	0.215
30 th (n = 31) ^b	0.221	0.456*	0.704 [†]	0.215	0.725 [†]	0.343

SGA: Appropriate for gestational age; VLBW: Very low birth weight; L/A: Length/age; W/L: Weight/length; HC: Cephalic circumference; MAC: Mid arm circumference; TC: Thigh circumference; SF: skin folds.

^aΣ4SF n = 14.

*p < 0.05; **p < 0.01; [†]p < 0.001.

^bTwo premature infants died and nine were discharged between the 14th and 30th day.

Table V
Multiple regression model^a of the z-score of weight/age as the dependent variable and anthropometric indicators of growth and nutritional status as the independent variables in 57 VLBW AGA premature infants and in 44 VLBW SGA premature infants

Independent variables	Regression coefficient (r)	Standardized coefficient (β)	p
<i>AGA premature infants</i>			
Head circumference (z)	0.250	0.344	<0.001
Thigh Circumference (z)	0.160	0.291	<0.001
Weight/length (z)	0.248	0.233	<0.001
Mid arm circumference (z)	0.103	0.206	0.005
Length/age (z)	0.158	0.187	0.015
$\Sigma 4$ Skin folds	0.175	0.162	0.045
<i>SGA premature infants</i>			
Thigh circumference (z)	0.320	0.561	<0.001
Head circumference (z)	0.272	0.415	<0.001
Mid arm circumference (z)	0.123	0.247	<0.001

VLBW: Very low birth weight (< 1,500 g); AGA: Adequate for gestational age; (z): z-score; ^aAdjusted R² 0.757; SGA: Small for gestational age; (z): z-score; ^aAdjusted R² 0.698.

show the correlation coefficients of the anthropometric indicators in the VLBW/AGA and VLBW/SGA premature infants. The W/A z-score was assigned as the dependent variable. All the indicators were also analyzed as z-scores.

Table V show the multiple regression models of the z-score of W/A as the dependent variable and the anthropometric indicators of growth and nutritional status as the independent variables in 57 VLBW/AGA and 44 VLBW/SGA premature infants. In the VLBW/AGA premature infants, HC was the major independent variable explaining the variability of the W/A index. In the VLBW/AGA premature infants, all the anthropometric indicators explained the variability on W/A (76%). In the VLBW/SGA premature infants, only three anthropometric indicators, TC, HC and MUAC, explained the variability of the W/A index (70%).

Discussion

This study showed that the probability of having a major number of significant correlations ($r > 0.5$) among anthropometric indicators was higher in the AGA premature infants than in the SGA premature infants. This outcome was particularly true at the initial and final stages of hospitalization. These results for the different weights for gestational age of VLBW premature infants can show two different situations. 1) The differences found in the growth and nutritional status on admission to the NICU continued until the end of four weeks of hospitalization. 2) The majority of the anthropometric indices of these VLBW premature infants ($\leq 1,500$ g) would be better markers of growth than of the nutritional status. However, the deceleration of growth in the early stage of life according to the

anthropometric indices could reflect inadequate nutritional conditions. This deceleration could be explained by other fetal or maternal factors (including oxygen restriction; maternal infection; drug addiction; and congenital and/or genetic diseases) not strictly related to insufficient and/or inadequate prenatal and postnatal nutrient intake.²⁴ This interpretation is reinforced by combining all the significant correlations ($r > 0.5$) among the anthropometric indices in the first 30 postnatal days. The probability of having a major number of significant correlations was higher in the AGA premature infants than in the SGA premature infants [OR = 2.7 (1.3, 5.6), $p = 0.006$].

These findings could indicate that there is a major congruence among the anthropometric indices when the VLBW premature infants grow normally compared with the premature infants who potentially suffered intrauterine growth restriction of intrinsic or extrinsic mono- or multi-factorial causes.²⁵⁻²⁷ This anthropometric profile tends to remain the same during hospitalization in the NICU because of mono- or multi-factorial causes.^{13,14}

It was evident that at admission and after seven days of hospitalization in the NICU, the observed significant correlations among the anthropometric indicators would explain the nutritional status and growth in the VLBW AGA premature infants. In these early stages of life and hospitalization, the less useful indicators would be those reflecting the incorporation of fat (weight/length and S4SF). Although, limitations of using these anthropometric measures as predictors of body fat should be recognized,^{28,29} and also, that skin-fold thickness only estimates subcutaneous fat.³⁰ The VLBW SGA premature infants could show different anthropometric characteristics, especially at the initial and first week of postnatal life. In this group, the W/A index is an indicator of growth and nutritional status.

Ehrenkranz et al.¹⁴ demonstrated significant positive correlations between the velocities of weight, length, HC, and MUAC gains, indicating that infants who tended to grow rapidly in one measure tended to grow rapidly in other measures. In this group of SGA premature infants, the inverse relationship observed between L/A and W/A indices at admission and at seven days appeared to reflect a non-harmonic growth with a more acute intrauterine restriction in the weeks close to delivery. These outcomes would coincide with a sub-jacent fetal and/or maternal pathology or might reflect those causes that triggered early delivery.²⁴ It was evident that at 14 and 30 days of hospitalization in the NICU, the VLBW SGA premature infants with probable intrauterine restriction would be affected by clinical conditions and/or insufficient nutrient and energy intake. This result causes significant correlations among the indicators of nutritional status and growth, including the W/A index, TC and HC.¹³

In the VLBW SGA premature infants and postnatal malnourished infants, MUAC was the only indicator that significantly correlated with S4SF, implying that MUAC would be a better indicator for evaluating nutritional recovery by the incorporation of subcutaneous fat. In those VLBW/AGA premature infants, HC was an important indicator that not only reflects the cerebral growth but also physical growth because it significantly correlated, during the hospitalization period, with the anthropometric indicators that better expressed growth (W/A, and L/A). At the time of hospitalization and after seven days of hospitalization in the NICU, the indicator HC of the VLBW/SGA premature infants showed non-significant correlations with the other anthropometric indicators. At 14 and 30 days, the correlations of HC with the other indicators of growth such as W/A, L/A, and TC were more significant. It is probable that clinical stabilization, especially in the later stages of hospitalization, with more stable nutrient and energy intake could have a favorable influence for showing more congruence among the different indicators of growth.

This outcome is significant because of the importance of weight gain and HC growth during the early neonatal period (during hospitalization in the NICU) for long-term neurodevelopment. Poor early neonatal HC growth has been associated with abnormal neurological examinations and abnormal mobility at the age of 5.4 years, and poor early neonatal weight gain has been associated with abnormal neurological examinations and lower mental processing composite scores in multiple regression models. These results could account for the relationship between perinatal risk factors and socioeconomic status.^{13,31}

The main limitation of the study would be related to the progressive decrease in the number of premature infants during the 30 days of the hospitalization period. However, the final sample (n = 80) that completed the period of study and statistical analysis was apparently sufficient.

In conclusion the results obtained in the final multiple regression analysis would indicate that the index of W/A (z) in the VLBW/AGA premature infants could reflect growth, nutritional status and energy stored as fat. In the VLBW/SGA premature infants, the TC and MUAC could be indicators of nutritional status, and the HC, besides its importance as an indicator for long-term neurodevelopment, could be an indicator of growth. The SF thickness and W/L anthropometric indicators would be less useful for the evaluation of nutritional status in the VLBW/SGA premature infants hospitalized in the NICU during the early days of life.

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Original / Valoración nutricional

Application of body mass index adjusted for fat mass (BMIfat) obtained by bioelectrical impedance in adults

Mirele Savegnago Mialich¹, Edson Zangiacomi Martinez² and Alceu Afonso Jordão Junior³

¹Post-doctoral Student. Department of Internal Medicine. Faculty of Medicine of Ribeirão Preto. University of São Paulo. Ribeirão Preto. SP, Brazil. ²Professor. Department of Social Medicine. Faculty of Medicine of Ribeirão Preto. University of São Paulo. Ribeirão Preto. SP, Brazil. ³Professor. Department of Internal Medicine. Faculty of Medicine of Ribeirão Preto. University of São Paulo. Ribeirão Preto. SP, Brazil.

Abstract

Introduction: Body mass index (BMI) has been one of the methods most frequently used for diagnose obesity, but it isn't consider body composition.

Objective: This study intends to apply one new adiposity index, the BMI adjusted for fat mass (BMIfat) developed by Mialich et al. (2011), in a adult Brazilian sample.

Methods: A cross-sectional study with 501 individuals of both genders (366 women, 135 men) aged 17 to 38 years and mean age was 20.4 ± 2.8 years, mean weight 63.0 ± 13.5 kg, mean height 166.9 ± 9.0 cm, and BMI 22.4 ± 3.4 kg/m².

Results and discussion: High and satisfactory R2 values were obtained, i.e., 91.1%, 91.9% and 88.8% for the sample as a whole and for men and women, respectively. Considering this BMIfat were developed new ranges, as follows: 1.35 to 1.65 (nutritional risk for malnutrition), > 1.65 and ≤ 2.0 (normal weight) and > 2.0 (obesity). The BMIfat had a more accurate capacity of detecting obese individuals (0.980, 0.993, 0.974) considering the sample as a whole and women and men, respectively, compared to the traditional BMI (0.932, 0.956, 0.95). Were also defined new cut-off points for the traditional BMI for the classification of obesity, i.e.: 25.24 kg/m² and 28.38 kg/m² for men and women, respectively.

Conclusion: The BMIfat was applied for the present population and can be adopted in clinical practice. Further studies are needed to determine its application to different ethnic groups and to compare this index to others previously described in the scientific literature.

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Correspondence: Mirele Savegnago Mialich.
Department of Internal Medicine.
Faculty of Medicine of Ribeirão Preto.
University of São Paulo.
Av. Bandeirantes 3900.
14049-900 Ribeirão Preto, Brazil.
E-mail: mirele.mialich@usp.br

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APLICACIÓN DEL ÍNDICE DE MASA CORPORAL PARA AJUSTAR LA MASA DE GRASA OBTENIDO POR IMPEDANCIA BIOELÉCTRICA EN ADULTOS

Resumen

Introducción: El índice de masa corporal (IMC) es uno de los métodos que se utilizan con mayor frecuencia para diagnosticar la obesidad, pero ese no considera la composición corporal.

Objetivo: Este estudio objetivó aplicar un nuevo índice de adiposidad, el IMC ajustado por la masa de grasa (BMIfat) desarrollado por Mialich et al. (2011), en una población adulta brasileña.

Métodos: Estudio transversal con 501 individuos de ambos sexos (366 mujeres y 135 hombres) entre 17 y 38 años, edad media de $20,4 \pm 2,8$ años, con una media de peso de $63,0 \pm 13,5$ kg, con una media de altura $166,9 \pm 9,0$ cm, y IMC $22,4 \pm 3,4$ kg/m².

Resultados y discusión: Se obtuvieron altos y satisfactorios valores de correlación (R2): 91,1% , 91,9% y 88,8% para la muestra en su conjunto y para los hombres y mujeres, respectivamente. Teniendo en cuenta este BMIfat se han desarrollado nuevas gamas, de la siguiente manera: 1,35-1,65 (riesgo nutricional para la malnutrición), > 1,65 y ≤ 2,0 (peso normal) y > 2,0 (obesidad). El BMIfat tiene una capacidad más precisa de detectar individuos obesos (0,980; 0,993; 0,974; considerando la muestra en su conjunto y las mujeres y los hombres, respectivamente), en comparación con el índice de masa corporal tradicional (0,932; 0,956; 0,95). También fueron definidos nuevos puntos de corte para el IMC tradicional para la clasificación de la obesidad: 25,24 kg/m² y 28,38 kg/m² para los hombres y mujeres, respectivamente.

Conclusión: El BMIfat se aplicó para la población actual y puede ser adoptado en la práctica clínica. Se necesitan más estudios para determinar su aplicación a los diferentes grupos étnicos y para comparar ese índice con otros descritos previamente en la literatura científica.

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Palabras clave: Composición corporal. Índice de masa corporal. Impedancia bioeléctrica. Grasa corporal.

Introduction

According to the World Health Organization (WHO), obesity is defined as excess adipose tissue.¹ Today obesity can be considered to be the most important nutritional disorder in developed countries; its incidence is believed to reach 10% of the population of these countries² and more than one third of the North American population is believed to be above the desirable weight. Thus, obesity is being considered to be a worldwide epidemic, present both in developed and developing countries.²

Brazil occupies 77th position in the WHO ranking; in 2010 the Health Ministry and the Brazilian Institute of Geography and Statistics (IBGE) published two large surveys of excess weight and obesity data in Brazil: the Vigilance of Risk Factors and Protection against Chronic Diseases by Telephone Interview (VIGITEL Brazil 2009), and the Survey of Family Budgets 2008-2009 (POF). The first survey revealed a frequency of excess weight of 46.6%, with a higher rate among men (51.0%) than among women (42.3%). This tendency was confirmed by the POF, which demonstrated that excess weight almost tripled among men from 18.5% in 1974-75 to 50.1% in 2008-09, and increased from 28.7% to 48% among women.

The index universally accepted for the classification of obesity is the body mass index (BMI) proposed by Quetelet in 1835, which is expressed as body weight in kg divided by height squared in meters (weight/height²). In 1997, the WHO adopted this index as a reference measurement of obesity, with overweight and obesity being defined as a BMI range of 25.0-29.9 kg/m² and a BMI above 30.0 kg/m², respectively. Since then, these cut-off points have been used as standards in different populations and different ethnic groups, based on the assumption that these different ethnic groups have similar risks of mortality/morbidity. However, recent studies^{3,4,5} have shown that there still is controversy about the best BMI for the classification of obesity in different populations.

In view of these problems regarding obesity, there is a pressing need to propose a refinement of the BMI by validating a new BMI adjusted for fat mass [(3 Weight + 4 Fat Mass) Height] previously developed by Mialich et al. (2011).³ There is also the need to develop new classification ranges for the adoption of this index in clinical practice.

Methods

Subjects

The study was conducted on healthy individuals of both genders, i.e., adolescents aged 17 years to 19 years, 11 months and 29 days and adults aged 20 years or older⁶ enrolled in undergraduate courses of the University of Sao Paulo (USP). The courses were

chosen at random and by convenience and all students of one class were invited to participate.

The students gave written informed consent to participate in the study (protocol n° 1955/2010) and all the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation. All the individuals were then submitted to measurement of weight and height and evaluation of body composition by bioelectrical impedance.

Exclusion criteria were: inability to walk, amputation, presence of metal objects in the body, difficulty in making the measurements, or interference with the results of bioelectrical impedance. The participation of the students was voluntary and all individuals were evaluated only once during the study by a group of trained examiners.

Anthropometric evaluation

Body weight (kg) was measured with an electronic scale (BC-558 Ironman Segmental Body Composition Monitor, Tanita Corp., Tokyo, Japan) with a maximum capacity of 150 kg and precision of 0.01 kg. Weight was measured after at least 5 hours of fasting, followed by bladder emptying, with the individuals wearing light clothing and no shoes. Height was measured with the aid of a wood bracket along a plastic tape fixed to a wall with no baseboard, with the subject standing up straight, barefoot and with head and neck aligned. Height (m) was measured twice with a maximum variation of 0.5 cm being permitted between measurements, and the mean of the two values was calculated.⁷ BMI was calculated as weight (kg) divided by height (m) squared (kg/m²). Criteria used to define overweight were the ones of the World Health Organization (WHO),¹ which considers obesity when BMI $\geq$ 30 kg/m².

Evaluation of body composition

Percentage of body fat mass was obtained by Tetrapolar Bioelectrical Impedance Analysis (BIA) system (BC-558 Ironman Segmental Body Composition Monitor, Tokyo, Japan). BIA measurements were carried out at 50 kHz with a 0.8 mA since wave constant current under standard conditions. Detailed instructions about electrode placements according to the manufacturer's manual were also provided.

For this exam, the individuals wore light clothing and no socks, with care taken to insure that their heels were correctly aligned with the electrodes of the measuring platform. The following requirements had to be fulfilled: fasting for at least 5 hours, no vigorous physical activity in the last 12 hours, wearing light clothing, urinating 30 minutes before the beginning of the exam, and abstaining from alcoholic or caffeine-

containing beverages for 12 hours before the exam. During the exam, the individuals held with their hands retractable levers with electrodes that functioned jointly with the foot electrodes, forming a 90° C angle between the base of the electrode and the rod connecting it to the equipment. After this measurement, which lasted approximately 30 seconds, the screen automatically presented the final result of the evaluation of body composition.

The new adiposity index (BMIfat) was calculated using the equation suggested by Mialich and colleagues (BMIfat) and weight in kg, fat mass in % and height in cm.³

Statistical analysis

For the analyses of the new index corrected for fat mass, regression models were adjusted, having the “new adjusted BMI” as the independent variable and the “traditional BMI” as the dependent variable, with the coefficient of determination (R²) being used as a measure of the predictive capacity of the “new adjusted BMI” compared to the “traditional BMI”.

For the elaboration of the ranges of nutritional status classification for this new adjusted BMI so that it could be adopted in clinical practice we used the classification ranges of the traditional BMI associated with cut-off points for body fat of 25% and 35% for men and women, respectively.¹

Considering the diagnostic performance of this BMIfat compared to the traditional BMI, it was calculated sensitivity, specificity, predictive values with their respective 95% and ROC curves (Receiver Operating Characteristic) for detecting areas under the curve, considering both BMI traditional as BMIfat for all individuals and separate gender. Simple linear regression was used for the definition of the new cut-off points of the BMI for the classification of obesity in this population. The Student was used to compare the means and analysis of variance (ANOVA) was used for the analysis of three means or more, with the level of significance set at $p < 0.05$ for both tests. All this analysis used the software SAS version 9.

Results

The sample consisted of 27.0% men and 73.0% women, 84.7% of them being white, 10.1% mulatto, 3.8% oriental, and 1.4% black. Mean age was 20.4 ± 2.8 years for the sample as a whole, 20.8 ± 3.2 years for men, and 20.3 ± 2.7 years for women, with no significant difference between groups.

The values of the variables weight, height and BMI were significantly higher for men (71.7 ± 18.5 kg, 169.6 ± 8.4 cm and 24.4 ± 3.8 kg/m², respectively) than for women (64.6 ± 16.0 kg, 157.2 ± 5.8 cm and 21.7 ± 3.0 kg/m², respectively).

Regarding the remaining body composition data, men had significantly higher values than women for fat-free mass (60.0 ± 7.7 kg *versus* 39.8 ± 3.8 kg) and total body water (59.9 ± 5.3 % *versus* 54.3 ± 4.4 %), whereas fat mass was greater in women (26.6 ± 6.2 % *versus* 17.0 ± 6.2 %). There was no statistically significant difference with respect to age among both gender (20.8 ± 3.2 years *versus* 20.3 ± 2.7 years for men and women, respectively) (table I).

The individuals studied were enrolled in the following courses: Medicine (n = 62), Nutrition (n = 98), Speech Therapy (n = 44), Physiotherapy (n = 75), Occupational Therapy (n = 27), Biomedical Informatics (n = 43), Physical Education (n = 59), and Nursing (n = 93). Most of them were single, were non-smokers, and were not employed, but were taking alcoholic drinks.

Linear regression models were used for analysis of the BMI adjusted for fat mass and the coefficient of determination (R²) was used as a measurement of the predictive capacity of the “adjusted BMI” compared to the “traditional BMI”. When the sample was considered as a whole, the R² was 91.1%, and when the individuals were divided according to gender, the R² was 91.9% and 88.8% for men and women, respectively.

One of the secondary objectives of the present study was to develop ranges of classification for this new index so that it could be used in clinical practice. In this respect, the sample data were distributed according to the ranges of the traditional BMI defined by the WHO¹ and according to the new values obtained after calculating the BMI adjusted for fat mass (fig. 1). It can be seen

Table I
Description of anthropometric and body composition of all subjects and separated by gender, male and female

	All (n = 501)	Male (n = 135)	Female (n = 366)	p value*
Age (years)	20,4 ± 2,8	20,8 ± 3,2	20,3 ± 2,7	0,0813
Weight (kg)	63,0 ± 13,5	76,9 ± 13,6	57,8 ± 9,2	<0,0001
Height (m)	166,9 ± 9,0	177,3 ± 6,7	163,1 ± 6,3	<0,0001
BMI (kg/m ²)	22,4 ± 3,4	24,4 ± 3,8	21,7 ± 3,0	<0,0001
FFM (kg)	45,3 ± 10,3	60,0 ± 7,7	39,8 ± 3,8	<0,0001
FM (%)	24,0 ± 7,5	17,0 ± 6,2	26,6 ± 6,2	<0,0001
TBW (%)	55,8 ± 5,2	59,9 ± 5,3	54,3 ± 4,4	<0,0001

*Comparisons the means between the genders with Student t-test and statistical significance if $p < 0.05$.

BMI: Body mass fat; FFM: Fat-free mass; FM: Fat mass; TBW: Total body water.

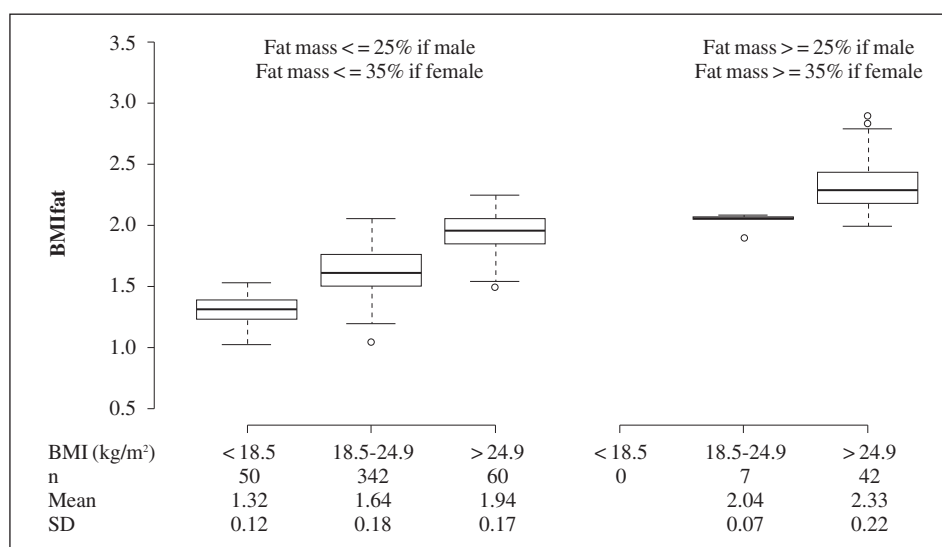


Fig. 1.—Subject distribution by gender according to the classification ranges for the traditional BMI, considering the corresponding values of adjusted BMI (BMI_{fat}) corresponding to cut-off points for fat mass of 35% and 25% for women and men, respectively.

that the suggested ranges of the adjusted BMI corresponding to the traditional BMI considering the sample as a whole would be: 1.35 to 1.65 (risk for malnutrition), > 1.65 and ≤ 2.0 (normal weight) and > 2.0 (obesity).

Considering the cut-off points for fat mass for the classification of obesity proposed by the WHO, i.e., 25% and 35% for men and women, respectively, it is possible to compare the capacity of the traditional

BMI and the capacity of the new adjusted BMI to detect obesity in the sample evaluated. It can be seen that the area under the curve for the adjusted BMI (0.980, 0.993, 0.974) was greater than that of the traditional BMI (0.932, 0.956, 0.95) for the classification of obesity considering the sample as a whole and divided into men and women, respectively (figs. 2 and 3).

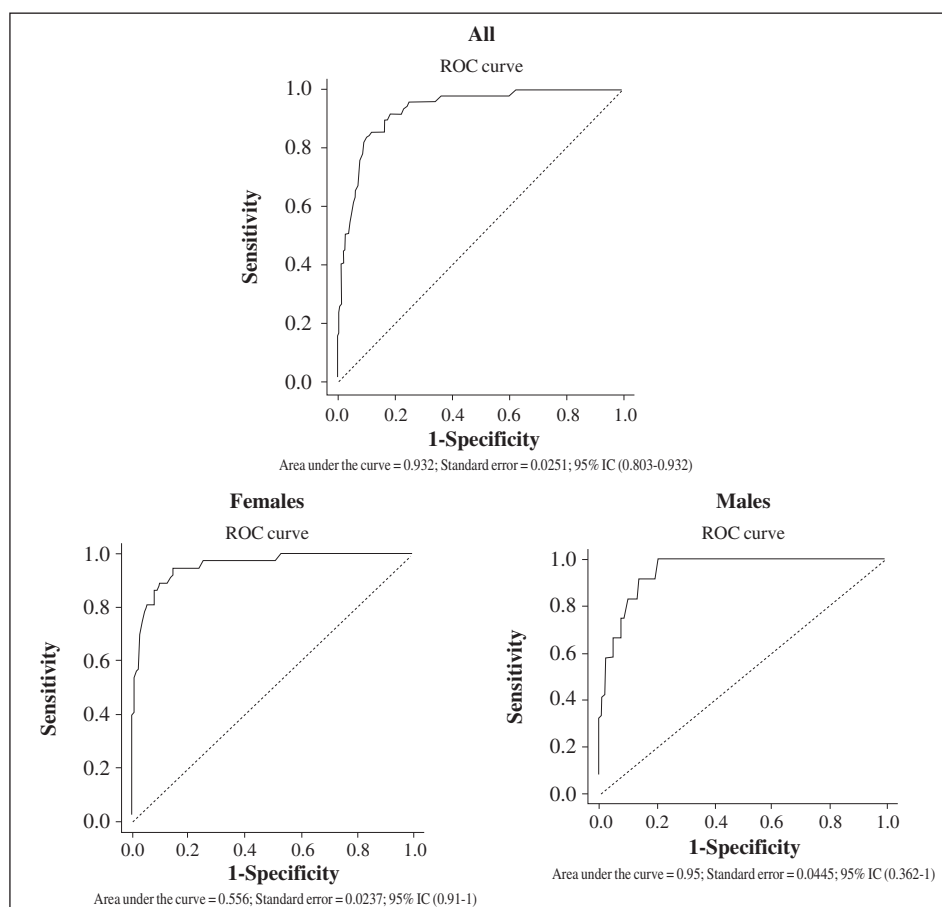


Fig. 2.—Subject distribution according to the cut-off points for body fat (25% for men and 35% for women) and traditional BMI values followed by their respective ROC curves, divided into the study group as a whole, and women and men, respectively.

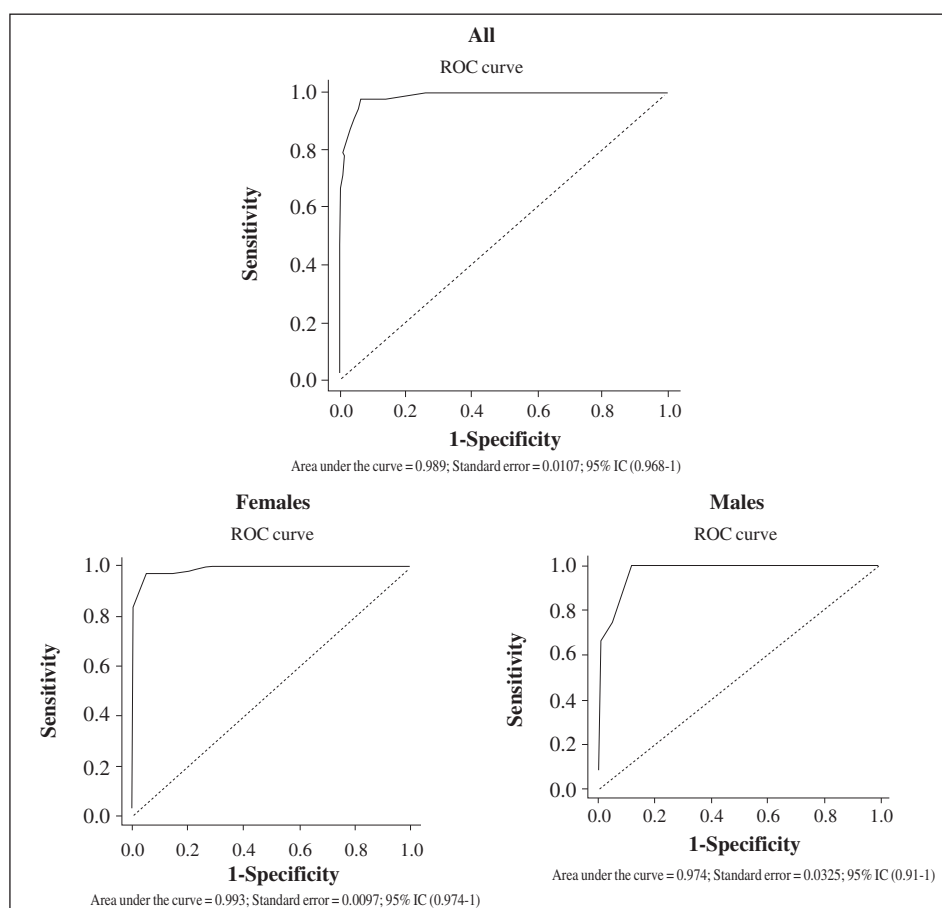


Fig. 3.—Subject distribution according to the cut-off points for body fat (25% for men and 35% for women) and BMI values adjusted (BMIfat) according to their respective ROC curves, divided into the study group as a whole, and women and men, respectively.

We also intended to propose new cut-off points for the BMI for the correct classification of nutritional status in the Brazilian population. For this purpose, we performed regression analysis and obtained new values of the traditional BMI for the detection of obesity in this sample, which were: 25.24 kg/m² (considering body fat = 35%) and 28.38 kg/m² (considering body fat = 25%) for women and men, respectively.

When the same analysis was carried out, but now considering the new adjusted BMI, the following new cut-off points were obtained: 1.85 (for body fat = 30%) and 2.1 (for body fat = 35%), both for women, and 1.8 (for body fat = 20%) and 2.08 (for body fat = 25%), both for men, as illustrated in Figure 4. It can be seen that the cut-off points for the BMI adjusted for the classification of overweight and obesity were closely similar for the two genders, underscoring one of the major advantages of this index, i.e., its uniform applicability to both genders, as illustrated in figure 4.

Discussion

The present study, conducted on a sample of the adult Brazilian population, demonstrated a limited diagnostic performance of the traditional BMI for the

correct identification of individuals with excess body fat and proposed the adoption of a BMI adjusted for fat mass [(3 Weight + 4 Fat Mass)/Height], which was applied for the sample under study as described earlier. However, the authors emphasize that new studies with randomized samples representative of the Brazilian population are still necessary.

Another objective of the present study in addition to application was to develop ranges of classification of the new index so that it could be applied to routine clinical practice. On this basis, we opted to describe ranges that would consider the sample as a whole since the major focus of the study was to keep the new index simple so that it could be applied to all individuals without any additional variable that would involve dividing the equation between men and women. Thus, in order to facilitate the use and interpretation of this adjusted index in clinical practice, we opted for the same adjusted BMI ranges for both genders (1.35 to 1.65, > 1.65 and ≤ 2.0, and > 2.0) that would correspond to those of the traditional BMI. At this time, we should point out the limitation of the present study due to the failure to adopt a gold standard technique for the comparison of the index, as done by Bergman et al. (2011), who opted for DXA for the validation of the Body Adiposity Index (BAI).⁸

In addition, the present study also proposes new cut-off points for the classification of obesity considering

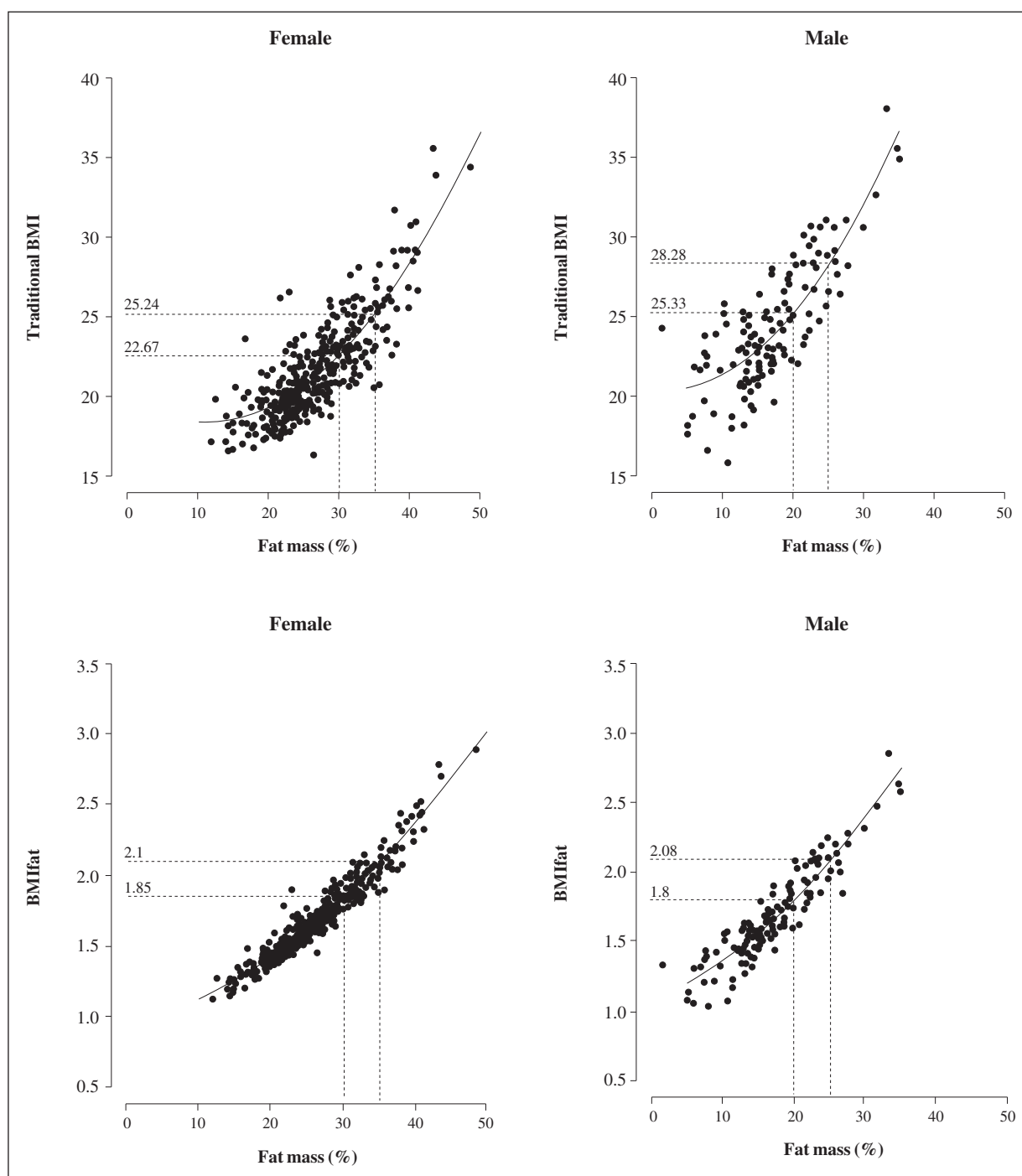


Fig. 4.—Cut-off point of the traditional BMI and the BMIfat for the detection of obesity in men and women of the sample studied, considering percentages of body fat for the classification of overweight and obesity of 20% and 25% and 30% and 35% for men and women, respectively.

35% body fat for women and 25% for men, corresponding to 25.24 kg/m² and 28.38 kg/m² for men and women, respectively.

Other studies have also been published in the literature to propose and discuss new cut-off points for the BMI for the classification of obesity in different ethnic groups, as shown by the comparative data presented in table II.^{3-4,9-20}

Among the limitations of this study, the authors acknowledge that the sample used was a sample of convenience, and this has limited applicability, especially for being composed of young people who have narrow bands for age and body composition. Moreover, they know that the method used to assess body composition, BIA, is not a method of reference. However, many studies have shown a high correlation

Table II
Comparative summary of studies proposing new cut-off points of BMI for the classification of overweight/obesity in men and women

Reference	Country	n	BMI cut off points - Men	BMI cut off points - Women
Deurenberg-Yap et al. (2000) ⁹	Singapore	291	26.0 to 27.0 kg/m ²	26.0 to 27.0 kg/m ²
Frankenfield et al. (2001) ¹⁰	USA	141	22.6 kg/m ²	20.1 kg/m ²
Ko et al. (2001) ¹¹	China	5153	23.0 – 26.0 kg/m ²	23.0 – 26.0 kg/m ²
Craig et al. (2001) ¹²	Australia	393	26.9 kg/m ²	24.5 kg/m ²
Dudeja et al. (2001) ¹³	India	123	21.5 kg/m ²	19.0 kg/m ²
Oh et al. (2004) ¹⁴	Korea	773.915	25.0 kg/m ²	25.0 kg/m ²
Kagawa et al. (2006) ¹⁵	Japan	139	–	23.0 kg/m ²
Bozkirli et al. (2007) ¹⁶	Turkey	909	28.24 kg/m ²	28.02 kg/m ²
Romero-Corral et al. (2008) ¹⁷	USA	13601	25.8 kg/m ²	25.5 kg/m ²
Laughton et al. (2009) ¹⁸	Canada	77	22.1 kg/m ²	22.1 kg/m ²
Mialich et al. (2011) ³	Brazil	200	21.84 – 26.11 kg/m ²	22.0 – 25.3 kg/m ²
Gupta e Kapoor (2012) ⁴	India	578	22.9 – 28.8 kg/m ²	22.9 – 28.8 kg/m ²
Gómez-Ambrosi et al. (2012) ¹⁹	Spain	6123	29.0 kg/m ²	27.0 kg/m ²
Laurson, Eisenmann and Welk (2011) ²⁰	USA	8268	Percentil 83	Percentil 80
Present study	Brazil	501	28.38 kg/m ²	25.24 kg/m ²

with data obtained by BIA and gold standard techniques such as DXA.²¹

The BIA has been adopted as an attempt to let the new index easy to be applied to the extent that you need cheap equipment, easy to use, portable and available in most institutions. Thus, associating other variables such as weight and height to the fat mass data obtained by BIA provides a refinement of the assessment of body composition.

Conclusion

Thus, even though the BMI is a measurement internationally adopted for the classification of nutritional status, it does not evaluate body composition since it does not differentiate between fat mass and fat-free mass, possibly leading to incorrect diagnoses and therefore erroneous clinical interventions. The proposed adjusted BMI (BMIfat) was applied for the present sample and showed diagnostic superiority for the classification of obesity compared to the traditional BMI. New BMI ranges adjusted for the classification of obesity in the adult Brazilian population were also proposed, permitting the inclusion of a larger number of individuals and consequently an earlier clinical intervention. Further studies are needed to determine the application of this BMIfat to different randomized ethnic groups and to compare its diagnostic performance to that of other indices previously described in the scientific literature.

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Original / Valoración nutricional State of malnutrition in hospitals of Ecuador

Sylvia Gallegos Espinosa¹, Marcelo Nicolalde Cifuentes¹, Sergio Santana Porbén²; for the Ecuadorian Group for the Study of Hospital Malnutrition*

¹School of Nutrition and Dietetics. Faculty of Public Health. Polytechnical School of Chimborazo. Riobamba. Chimborazo. Ecuador. ²Vicepresidency. Board of Governors. Cuban Society of Clinical Nutrition and Metabolism.

*The composition of the Ecuadorian Group for the Study of Hospital Malnutrition is presented in the Annex to this document.

Abstract

Rationale: Hospital malnutrition is a global health problem affecting 30-50% of hospitalized patients. There are no estimates of the size of this problem in Ecuadorian hospitals. Hospital malnutrition might influence the quality of medical assistance provided to hospitalized populations.

Objectives: To estimate the current frequency of malnutrition among patients admitted to Ecuadorian public hospitals.

Materials and methods: The Ecuadorian Hospital Malnutrition Study was conducted between November 2011 and June 2012 with 5,355 patients (Women: 37.5%; Ages ≥ 60 years: 35.1%; Length of stay ≤ 15 days: 91.2%) admitted to 36 public hospitals located in the prominent cities of 22 out of the 24 provinces of the country. Malnutrition frequency was estimated by means of the Subjective Global Assessment survey.

Results: Malnutrition affected 37.1% of the surveyed patients. Malnutrition was dependent upon patient's age and education level; as well as the presence of cancer, sepsis, and chronic organic failure. Hospital areas showed different frequencies of hospital malnutrition. Health condition leading to hospital admission influenced negatively upon nutritional status. Malnutrition frequency increased as length of stay prolonged.

Conclusions: Malnutrition currently affects an important proportion of patients hospitalized in public health institutions of Ecuador. Policies and actions are urgently required in order to successfully deal with this health problem and thus to ameliorate its negative impact upon quality of medical care.

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Key words: Hospital malnutrition. Length of stay. Epidemiology. Cancer. Subjective Global Assessment.

Correspondence: Sylvia Gallegos Espinosa.
School of Nutrition and Dietetics.
Faculty of Public Health.
Polytechnical School of Chimborazo.
Riobamba. Chimborazo. Ecuador.
E-mail: sylvia10@hotmail.com

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ESTADO DE LA DESNUTRICIÓN EN LOS HOSPITALES DEL ECUADOR

Resumen

Justificación: La desnutrición hospitalaria constituye un problema global de salud pública que afecta entre el 30-50% de los internados. En el Ecuador no se tienen estimados de la magnitud de este problema. La desnutrición hospitalaria pudiera influir en la calidad de la prestación de asistencia médica a la población hospitalizada.

Objetivos: Estimar la frecuencia corriente de desnutrición entre los pacientes internados en los hospitales públicos del Ecuador.

Material y Método: El Estudio Ecuatoriano de Desnutrición Hospitalaria se condujo entre Noviembre del 2011 y Junio del 2012 en 5,355 pacientes (Mujeres: 37,5%; Edades ≥ 60 años: 35,1%; Estadía ≤ 15 días: 91,2%) internados en 36 hospitales públicos ubicados en las ciudades cabeceras de 22 de las 23 provincias del país. La frecuencia de desnutrición hospitalaria se estimó mediante la Encuesta Subjetiva Global.

Resultados: La desnutrición afectó al 37,1% de los pacientes encuestados. La desnutrición fue dependiente de la edad y la escolaridad del enfermo; y la presencia de cáncer, sepsis, y falla orgánica crónica. Las áreas de hospitalización difirieron entre sí respecto de la frecuencia observada de desnutrición hospitalaria. El problema principal de salud influyó en el estado nutricional del enfermo. La frecuencia de desnutrición se incrementó a medida que se prolongó la estadía hospitalaria.

Conclusiones: La desnutrición afecta actualmente a una parte importante de los hospitalizados en las instituciones públicas del Ecuador. Urge la adopción de políticas y acciones para lidiar exitosamente con este problema de salud y de esta manera aminorar el impacto negativo del mismo sobre la calidad de la atención médica.

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Palabras clave: Desnutrición hospitalaria. Estadía hospitalaria. Epidemiología. Cáncer. Encuesta Subjetiva Global.

Introduction

Hospital malnutrition has been regarded as a global health problem with important social, economical, political and ethical overtones.¹⁻² As of today, malnutrition affects 30-50% of patients admitted to any hospital in the world.³ Malnutrition might be independent of social and economical features of a particular country.³ Malnutrition accompanies health condition leading to admission, increases as hospital length of stay prolongs, and represent an important cause of therapeutic failures, post-surgical complications, and even death.⁴⁻⁶ Above all, malnutrition might be the cause for increased costs of medical care.⁷

FELANPE (a Spanish acronym standing for *Federación Latinoamericana de Terapia Nutricional, Nutrición Clínica y Metabolismo**, or Latin American Federation of Nutritional Therapy, Clinical Nutrition and Metabolism[†]) conducted the ELAN Latin American Nutrition Study during 1999-2001, in order to establish malnutrition frequency among patients admitted to the region's public hospitals.⁸ The ELAN Study revealed that half of the hospitalized patients were malnourished at the time of the survey.⁸

Every disease has metabolic and nutritional components, and could place the patient at increased risk of malnutrition.⁹⁻¹⁰ Latin America still suffers from the social debt accumulated during the 1990s, so hospital malnutrition might include a socio-economic component dictated by the place the patient occupies within the economical, productive and social structures of the country.¹¹⁻¹² But the so-called hospital cultural practices as identified by Butterworth in 1973¹³ are the ones that could significantly affect patient's nutritional status and distort his/her response to medical and/or surgical actions.

The Ministry of Public Health (MINSAP) of the Republic of Ecuador sustains a hospital national network comprised of more than 50 institutions distributed among the 24 provinces of the country (Galápagos islands included). As of today, there are no systematic estimates of the extension of malnutrition among MINSAP institutions. Past efforts in this direction at a public hospital of the south of the city of Quito are to be duly noted.¹⁴

Effective health public policies can not be developed if extension and magnitude of hospital malnutrition are not taken into account. The School of Nutrition and Dietetics of the Faculty of Public Health located at the ESPOCH (a Spanish acronym standing for *Escuela Superior Politécnica del Chimborazo*, or Higher Polytechnical School of Chimborazo) has conducted the Ecuadorian Study of Hospital Malnutrition^{*} in order to determine the current frequency of malnutrition in public hospitals of the Republic of Ecuador.

^{*}Formerly the Latin American Federation of Parenteral and Enteral Nutrition.

[†]From here onwards referred as the Ecuador ELAN Study.

Material and method

Study design: Non-experimental, multi-center, cross-sectional, analytical type.

Study location: Hospital institutions eligible from the MINSAP's network of public hospitals. Public institutions located in the capitals of the 24 provinces of the Republic of Ecuador with 100 (or more beds) were selected. Selected hospitals from the IESS (a Spanish acronym for *Instituto Ecuatoriano de Seguridad Social*, or Ecuadorian Institute of Social Security) participated also in this study. Informed consent from the Board of Directors was obtained for including the institution in the present study.

Study subjects: Patients with ages ≥ 18 years hospitalized between November 2011 and June 2012 (at the time the survey took place), and consented with participating in the study after being informed about the purposes, objectives and procedures of the survey, were eligible for inclusion. Those patients who did not provide their consent, or in whom procedures prescribed in the study design were not completed, were excluded from the study.

From each patient sex (Male/Female), age (< 60 years / ≥ 60 years), health condition leading to admission, hospitalization area, admission date, and education level (Grammar/Junior High/High School/University/Senior Technician), were obtained. A sixth, additional "Undetermined" category was created within the education level variable in order to include those patients that did not complete the six grades of grammar school, were illiterates; or did not declare any level of instruction whatsoever.

Additional queries were made in order to establish if the patient had been operated upon (Surgery completed), was placed on waiting list (Surgery programmed), or no surgical treatment had been considered at all (Surgery not considered).

Sample size considerations: It was estimated goals of the survey would be met with a sample of 6,489 patients. Size of study sample was calculated in order to achieve the estimate of a proportion (in this case, the frequency of malnutrition in Ecuadorian hospitals) in an infinite population with a 95% statistical confidence and a 1.5% imprecision. A 50.0% malnutrition frequency was anticipated, according with the ELAN Study results.⁸

Selection of the study subjects in the analysis units: Subjects surveyed in each of the analysis unit (that is: the participating hospital) were selected by means of a systematic, (pseudo)random sampling of hospital beds. An assignation number of 2 was foreseen, thus recommending surveying one patient for every second occupied bed. This prescription was considered feasible to observe in larger hospitals with more than 100 beds. It was then recommended to collect data from 150 patients in each participating hospital in order to meet the set size of the sample study.

Beds were sequentially numbered until exhaustion of hospital's allocation. Sorted numbers (corresponding with surveyed patients) were paired with respective beds. On the day of the survey, the surveyor administered the procedures of the study to the first occupied bed. In case the bed to be surveyed was unoccupied, or the patient unable to complete the procedures of the survey in view of his/her clinical condition, patient occupying the bed following clockwise was surveyed.

Collected data were voided in the corresponding forms, and entered into an *ad hoc* digital container created with Access 7.0 of Office for Windows (Microsoft, Redmond, Virginia, USA).

Survey procedures: The Subjective Global Assessment (SGA) of the nutritional status proposed by Detsky et al.¹⁵ was administered to each of the surveyed patients. According with the subjective perception of the surveyor, the patient was assigned to any of three different nutritional categories: A: *Not Malnourished*, B: *Mildly Malnourished/At risk of malnutrition*, and C: *Severely Malnourished*, respectively.

At the same time, an audit of the nutritional care processes was conducted by means of the Hospital Malnutrition Survey (HMS). Briefly, HMS holds sections for recording the patient's sociodemographic and administrative data, current health conditions (emphasizing sepsis and cancer diagnoses), completion of major surgical procedures, occurrence of fasting, current state of provision of foods by mouth and the use of dietetic supplements, conduction of enteral nutrition schemes, and conduction of parenteral nutrition schemes; respectively. HMS results are to be discussed in a complementary article[‡].

Surveyors were instructed in survey's procedures by means of Standard Operating Procedures drafted for these purposes.¹⁶⁻¹⁷

Ethical considerations: Procedures conducted on patients were non-invasive in nature. Patients were informed by local surveyors of study's design, and characteristics of tools to be administered; and made aware of their freedom when choosing on their inclusion in the study. Patients were also informed about the confidentiality of data collected from them by local surveyors as part of the procedures of the study.

A Bioethics Committee at ESPOCH reviewed the project and requested provisions from the Ecuadorian Group for the Study of Hospital Malnutrition regarding the non-invasiveness of procedures to be conducted and proper storing of data to be collected.

Boards of Governors of eligible hospitals were approached by the Group for permission to conduct the study with patients admitted to the institution. Local surveyors presented the Boards with the design, purposes, and possible results of the study. Boards

were made aware of their freedom when deciding about the inclusion of the institution in the study.

Permission from the Board of Governors to interview the patients, as well as to store and manipulate data collected from them, was sought in the form of an informed consent as a prerequisite for conducting the survey at eligible hospitals. Additionally, the institution's Bioethics Committee was consulted by the Board of Governors about the features of the study.

The present work was aimed to show the integrated state of malnutrition in medical centers of different provinces of the Republic of the Ecuador. In any moment an attempt was made to expose malnutrition in a single hospital, and thus, a particular province. Hospitals's Boards were reassured about the confidentiality of the collected data, the proper storing of data, and the integrated nature of the results to be obtained.

Data processing and statistical-mathematical analysis of results: Collected data were reduced down to location (mean), dispersion (standard deviation) and aggregation (absolute frequencies/percentages) statistics, according with variable type.

Malnutrition frequency was obtained as the percentage of SGA surveys with (B + C) scores regarding the total number of recovered surveys. Malnutrition frequency was adjusted for age, sex, education level, health condition, infection (Present/Absent), surgical treatment, hospitalization area, and hospital length of stay (LOS). LOS was calculated as the number of days between date of the survey and admission date, and was distributed as follows: < 24 hours, From 2-3 days, From 4-7 days, From 8-15 days, From 16-30 days, and > 30 days; respectively.

Patient's health condition was categorized as follows: *Hematological diseases:* Anemias in different stages of diagnosis and treatment; *Chronic liver disease* (Liver cirrhosis included); *Cancer* (leukemias and lymphomas were also added); *Chronic kidney disease;* *Respiratory diseases* (tuberculosis, pneumonia, chronic obstructive pulmonary disease and bronchiectasia included); *Diabetes mellitus;* *Heart and blood vessels* (comprising heart and valves diseases, those derived/caused by atherosclerosis, and local I systemic venous insufficiency); *Gastrointestinal diseases* (major acute abdominal pain dramas included); *Gynecological diseases;* *Urological diseases;* *Burns;* *Orthopedic and trauma illnesses* (comprising fractures, trauma and wounds caused by weapons regardless of their type or nature); and *Neurological and psychiatric diseases* (dementia included); respectively. An "Others" additional category was created for those health problems not covered by the preceding categories.

Hospitalization area was stratified as follows: *General Surgery, Other surgical specialties, Orthopedics and Trauma, Internal Medicine, and Other medical specialties;* respectively.

Statistical significance of hypothesized differences was assessed by means of homogeneity tests based on

[‡]Nicolalde Cifuentes M, Gallegos Espinosa S, Santana Porbén C. The state of the processes of nutritional care in hospitals of Ecuador. Drafted for publication.

Table I
Participating hospitals. City, province, number of beds, and surveyed patients

<i>Province</i>	<i>Hospital</i>	<i>Number of beds</i>	<i>Surveyed patients</i>
Azuay	Hospital “Vicente Corral Moscoso”	290	150
Azuay	Hospital IESS “José Carrasco Arteaga”	300	150
Bolivar	Hospital “Alfredo Noboa Montenegro”	120	150
Bolivar	Hospital IESS “Humberto del Pozo Santos”	130	150
Cañar	Hospital “Homero Castanier Crespo”	160	150
Cañar	Hospital “Darío Machuca Palacios”	165	152
Carchi	Hospital “Luis Gabriel Davila”	150	150
Cotopaxi	Hospital “Central de Latacunga”	200	150
Chimborazo	Hospital “Docente de Riobamba”	220	149
Chimborazo	Hospital IESS Riobamba	180	150
El Oro	Hospital “Teófilo Davila”	220	150
Esmeraldas	Hospital “Delfina Torres de Concha”	125	155
Guayas	Hospital “Abel Gilbert Pontón”	254	149
Guayas	Hospital Neumológico “Alfredo J. Valenzuela”	340	150
Imbabura	Hospital San Vicente de Paul	166	150
Loja	Hospital IESS “Manuel Ignacio Monteros”	81	150
Loja	Hospital Regional “Isidro Cueva”	243	150
Los Ríos	Hospital “Martín Icaza”	106	103
Los Ríos	Hospital IESS Babahoyo	120	150
Los Ríos	Hospital del Sagrado Corazón de Jesús	71	150
Los Ríos	Hospital “Nicolás Coto Infante”	51	150
Manabí	Hospital “Rafael Rodríguez Zambrano”	220	150
Manabí	Hospital Hospital IESS Manta	120	149
Manabí	Hospital “Verdi Ceballos Balda”	305	150
Manabí	Hospital “Miguel H. Alcívar”	120	149
Morona Santiago	Hospital de Macas	70	150
Napo	Hospital “José María Velasco Ibarra”	120	150
Orellana	Hospital “Francisco de Orellana”	30	150
Pastaza	Hospital de Puyo	35	149
Pichincha	Hospital IESS “Carlos Andrade Marin”	720	150
Pichincha	Hospital “Eugenio Espejo”	470	150
Pichincha	Hospital “Pablo Arturo Suárez”	220	150
Santo Domingo de las Tsachilas	Hospital “Gustavo Domínguez”	141	150
Tungurahua	Hospital Nuestra Señora de la Merced	55	150
Tungurahua	Hospital Provincial Docente de Ambato	386	150
Tungurahua	Hospital IESS Ambato	360	150

Size of the study serie: 5355.

Source: Records of the Ecuadorian ELAN Study of Hospital Malnutrition.

Records closed on: December 31th, 2012.

the chi-square distribution.¹⁸ A probability of occurrence of the event lower than 5% was assumed as statistically significant.¹⁸

Strength of associations between nutritional status and variables included in the study’s experimental design was assessed indistinctively by means of techniques based on the chi-square distribution,¹⁸ or logistic regression.¹⁹

EPI-INFO (Centers for the Diseases Control. Atlanta: Georgia) and SPSS (SPSS Inc., Chicago, IL, EEUU) statistical packages were used for the statistical analysis of the results.

Results

Final sample size was 5,355 patients: a figure representing 82.5% of the goal set by survey design. These patients were surveyed in 36 hospitals of 23 (out of 24 of the) provinces of the country. Table I shows the hospitals surveyed as part of the Ecuador ELAN Study.

Table II shows the demographic and clinical features of the sample study. Women were more represented than men. Patients with ages ≥ 60 years represented a third of the sample. Grammar and junior high education levels were prevalent among the surveyed patients.

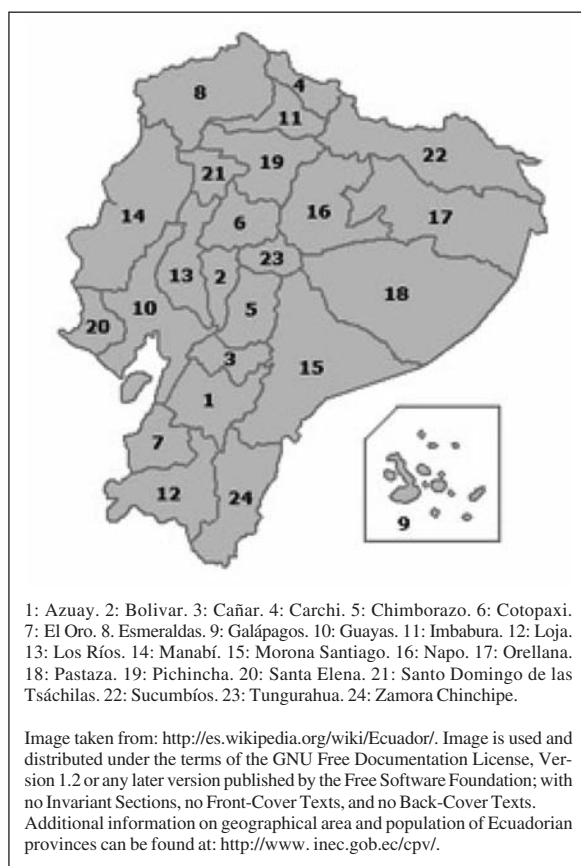


Fig. 1.—Provinces of Ecuador. The country is comprised of 24 provinces distributed between the Pacific coast, the Andes, and the Amazonia. Ecuador holds a population of 14,483,499 inhabitants over a 283,520 squared kilometers area.

Roughly 10.0% of the patients were included within the “Undetermined” category of education.

General Surgery (32.6%) and Internal Medicine (51.7%) services concentrated the surveyed hospitalizations. More than 90.0% of the patients had stayed at least 15 days in hospital. Gastrointestinal diseases, orthopedic and trauma illnesses, and respiratory illnesses concentrated 53.0% of the patients in the study sample. Infection was present in a quarter of the surveyed patients, mostly from the very moment of hospital admission. Cancer affected only 3.4% of the sample. Chronic organic failure was present in 8.2% of the patients. More than 20.0% of the patients had been already operated upon, while another 9.2% was waiting for completion of surgical program.

Estimated frequency of hospital malnutrition was 37.1% (95% CI: 35.8%-38.4%). According with SGA score, patients were distributed as follows: “A”: 63.0%; “B”: 29.1%; and “C”: 7.9%; respectively, as shown in figure 2.

Table III shows the association between SGA score and Body Mass Index (BMI) current value calculated for 4,884 of the surveyed patients (amounting to 91.2% of study sample). A strong association was found between SGA score and BMI current value: 84.2% of

the patients with (B + C) SGA scores had BMI values < 18.5 Kg.m⁻², in contrast with only 33.8% of those with “A” scores (OR = 10.48; $p < 0.05$; 95% CI: 7.75-14.19).

Table IV shows the influence of demographic and clinical features of the patient upon SGA score. SGA score was dependent upon age (< 60 years: 30.9% vs. ≥ 60 years: 48.5%; $D = -17.6\%$; $\chi^2 = 162.0$; $p < 0.05$) and education level ($\chi^2 = 99.75$; $p < 0.05$). Malnutrition concentrated among patients with grammar and junior high levels of instruction, as well as those included within the “Undetermined” category (OR = 0.812; $p < 0.05$; 95% CI: 0.773-0.851; odds-ratio estimated by means of logistic regression techniques). Likewise, hospital malnutrition was influenced by presence of cancer (Present: 64.5% vs. Absent: 36.1%; $D = 28.4\%$; $\chi^2 = 61.0$; $p < 0.05$), infection (Present: 47.8% vs. Absent: 33.5%; $D = 14.3\%$; $\chi^2 = 88.60$; $p < 0.05$), and chronic organic failure (Present: 58.2% vs. Absent: 35.2%; $D = 23.0\%$; $\chi^2 = 91.48$; $p < 0.05$); respectively.

In addition, patients going through different stages of surgical program differed among them regarding the observed frequencies of malnutrition ($\chi^2 = 119.51$; $p < 0.05$), being the proportion of (B + C) SGA scores higher in those in whom no surgical option of treatment was considered.

Table V shows the distribution of hospital malnutrition in relation to hospitalization area. Hospital areas exhibited varying malnutrition frequencies ($\chi^2 = 144.22$; $p < 0.05$), with higher frequencies among wards of Internal Medicine and other medical specialties.

Table VI shows malnutrition regarding health condition leading to admission. Malnutrition was heterogeneously distributed among different health conditions ($\chi^2 = 395.79$; $p < 0.05$). Observed estimates of malnutrition for hematological diseases, chronic liver diseases (including liver cirrhosis), cancer, kidney chronic disease, respiratory illnesses and Diabetes mellitus surpassed the globally estimated value for the study sample.

Finally, figure 3 shows the influence of hospital LOS upon nutritional status. Malnutrition frequency increased as LOS prolonged, from an initial value of 31.2% in the first 24 hours of hospitalization, to reach 64.7% among those patients with LOS between 16-30 days ($D = 33.5\%$; $p < 0.05$).

Discussion

This article has presented the results of the Ecuadorian Study of Hospital Malnutrition: the first concerted effort aimed to expose the magnitude and ramifications of this health problem in public health institutions of the country. As such, the Ecuador ELAN Study distincts itself from others conducted in the Latin american region for encompassing the public medical care centers of all (but one of) the provinces of the country; and for being the culmination of a Mastery in Nutrition

Table II
Demographical and clinical features of the surveyed population. Numbers and (between brackets) percentages of subjects for the corresponding level of distribution are shown

<i>Feature</i>	<i>Observed findings</i>
Sex	Female: 2756 [51.5] Male: 2599 [48.5]
Age	< 60 years: 3474 [64.9] ≥ 60 years: 1881 [35.1]
Education level	Grammar: 2770 [51.7] Junior high: 1395 [26.1] High school: 118 [2.2] University: 441 [8.2] Senior technician: 62 [1.1] Undetermined: 569 [10.6]
Health condition leading to admission	Gastrointestinal diseases: 1396 [26.1] Orthopedic and trauma illnesses: 790 [14.7] Respiratory diseases: 654 [12.2] Heart and blood vessels: 525 [9.8] Diabetes mellitus: 460 [8.6] Urological illnesses: 411 [7.7] Neurological and psychiatric illnesses: 190 [3.5] Cancer, leukemias and lymphomas: 180 [3.4] Chronic kidney disease: 139 [2.6] Chronic liver disease: 67 [1.3] Gynecological illnesses: 68 [1.3] Burns: 40 [0.7] Hematological diseases: 33 [0.6] Others*: 402 [7.5]
Infection [§]	Present: 1338 [25.0] • Present on admission: 1323 [98.9] • Developed during admission: 15 [1.1]
Organic chronic failure	Present: 438 [8.2]
Surgical program	Completed: 1197 [22.3] Programmed: 498 [9.3] Not considered: 3660 [68.4]
Hospitalization area	General Surgery: 1748 [32.6] Other surgical specialties [†] : 129 [2.4] Orthopedics and Trauma: 336 [6.3] Internal Medicine: 2769 [51.7] Other medical specialties [‡] : 373 [7.0]
Length of stay	Up to 24 hours: 1142 [21.3] Between 2-3 days: 1875 [35.0] Between 4-7 days: 1226 [22.9] Between 8-15 days: 641 [12.0] Between 16-30 days: 289 [5.4] More than 30 days: 182 [3.4]

*Hernia of varying etiology | topology (168), snake biting (40), HIV/aids (53), dengue (26).

[§]HIV/aids cases are included.

[†]Urology (44), Neurosurgery (43), Cardiovascular surgery (31), Otorhinolaryngology (9), Ophthalmology (2).

[‡]Gastroenterology (91), Cardiology (68), Neumology (57), Nephrology (51), Neurology (31), Endocrinology (26), Oncology (23), Infectology (18), Dermatology (4), Hematology (3), Psychiatry (1).

Size of the study serie: 5355.

Source: Records of the Ecuadorian ELAN Study of Hospital Malnutrition.

Records closed on: December 31th, 2012.

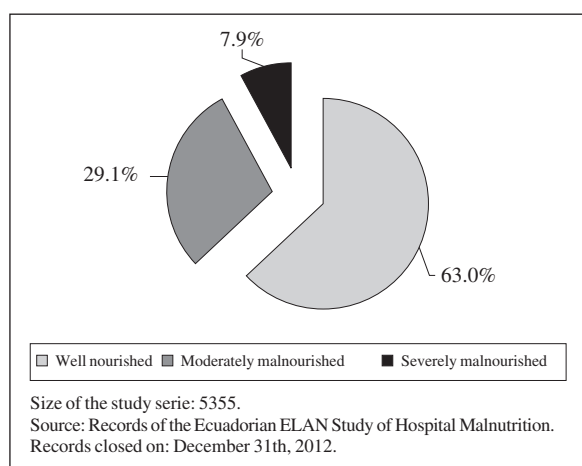


Fig. 2.—State of hospital malnutrition. Hospital malnutrition frequency was calculated from the proportion of patients with (B + C) SGA scores.

in Public Health project led by the School of Nutrition and Dietetics of the Faculty of Public Health at the ESPOC in Riobamba (Chimborazo) with the students acting as surveyors in the research units.

The estimated frequency of hospital malnutrition is consistent with findings previously reported by the

Table III

Association between Body Mass Index (BMI) and Subjective Global Assessment (SGA) score. Data recovered from 4,884 patients was distributed according with BMI calculated value and score assigned with SGA. Nature of association was assessed by means of statistical tests based on the chi-square distribution.¹⁸ Strength of association was estimated after calculation of the corresponding odds-ratio.¹⁸ Proportions of patients with a specified SGA score with BMI values on one side or the other of the selected cut-off point are shown

BMI, Kg.m ²	SGA		Totals
	B + C	A	
< 18.5	278 [84.2]	52 [15.8]	330 [6.7]
≥ 18.5	1538 [33.8]	3016 [66.2]	4554 [93.3]
Totals	1816 [37.2]	3068 [62.8]	4884 [100.0]

$\chi^2 = 335.564952$; $p < 0.05$.

OR = 10.4837 [7.7477-14.1861]

Size of the study serie: 5355.

Source: Records of the Ecuadorian ELAN Study of Hospital Malnutrition.

Records closed on: December 31th, 2012.

Table IV

Influence of demographical and clinical features of the patient upon the nutritional status of the patient

Feature	(B + C) score [§]	Interpretation
Sex		
• Male	37.5	$\chi^2 = 0.39$; $p > 0.05$ OR _J = 0.9651 [0.8637-1.0784]
• Female	36.6	
Age		
• < 60 years	30.9	$\chi^2 = 162.57$; $p < 0.05$ OR _J = 2.1089 [1.8787-2.3673]
• ≥ 60 years	48.5	
Education level		
• Grammar	40.6	$\chi^2 = 99.57$; $p < 0.05$ OR _L = 0.812 [0.773-0.851]
• Junior high school	30.2	
• High school	24.6	
• University	27.2	
• Senior technician	27.4	
• Undetermined	47.6	
Presence of cancer	64.5	$\chi^2 = 62.39$; $p < 0.05$ OR _J = 3.2905 [2.4098-4.4931]
Presence of sepsis	47.8	$\chi^2 = 87.70$; $p < 0.05$ OR _J = 1.8161 [1.6016-2.0594]
Presence of chronic organic failure	58.2	$\chi^2 = 91.66$; $p < 0.05$ OR _J = 2.5693 [2.1063-3.1341]
Stage of the surgical plan		
• Completed	29.0	$\chi^2 = 118.795$; $p < 0.05$ OR _L = 0.721 [0.672-0.774]
• Programmed	21.7	
• Not considered	41.8	

[§]Proportion of patients with (B + C) SGA scores in each level of distribution of the corresponding category.

OR_J: Odds-ratios estimated by means of chi-square techniques.¹⁸ OR_L: Odds-ratios estimated by means of logistic regression.¹⁹

Size of the study serie: 5355.

Source: Records of the Ecuadorian ELAN Study of Hospital Malnutrition.

Records closed on: December 31th, 2012.

Table V
Distribution of malnutrition regarding hospitalization area

Hospitalization area	(B + C) score ^s
General Surgery	30.6
Other surgical specialties	33.3
Orthopedics and Trauma	16.1
Internal Medicine	43.2
Other medical specialties	41.8
All areas	37.1

$\chi^2 = 143.72$; $p < 0.05$.

^sProportion of patients with (B + C) SGA scores in each surveyed area.

Size of the study serie: 5355.

Source: Records of the Ecuadorian ELAN Study of Hospital Malnutrition.

Records closed on: December 31th, 2012.

ELAN Latin American Hospital Nutrition Study.⁸ In a chaotic, hardly intervened scenario, it can be anticipated that between 30-50% of hospitalized patients are malnourished, as this study has shown.

Malnutrition concentrated among patients with ages ≥ 60 years, as well as those diagnosed with cancer, infection, and organic chronic failure. Aging affects the capacity of the human being to adapt and respond successfully to injury.²⁰ Illness, and the events it unleashes, might convey a nutritional and metabolic cost overriding the homeostatic mechanisms of the aging subject.²¹ Vulnerability and frailty of the family, community and social networks might also affect the capacity of the elder to sustain his/her nutritional status by himself/herself.²²⁻²³

Influence of cancer upon nutritional status has been extensively recognized. Malnutrition is present in 20-25% of the patients newly diagnosed with cancer, but it can become a highly prevalent phenomenon among those going through the several stages of the treatment of the neoplastic disease, as well as those submitted for palliative care.²⁴⁻²⁶

Infection can unleash | perpetuate | aggravate malnutrition that underlies in the hospitalized patient. Infection puts in motion molecular, biochemical and hormone events that result in inflammation, insulin resistance and hypercatabolism.²⁷⁻²⁸ Wasting syndromes associated with HIV/aids²⁹⁻³⁰ and tuberculosis cachexia³¹⁻³² are illustrative examples of the aforementioned. Regarding the present study serie, patients affected with HIV/aids and tuberculosis represented 3.7% and 9.9%; respectively; but malnutrition affected 84.0% of the formers, and 94.0% of the latters.

Chronic organic failure deeply alters the maintenance of the internal milieu of the patient, and thus, the way metabolic events required for the use of energy contained in foods operate.³³⁻³⁵ Chronic inflammation is also part of the biochemical events that organic chronic failure sets in motion. The elevated malnutrition rates observed in patients with end-stage kidney disease, chronic liver disease and chronic heart disease are a permanent reminder of the consequences brought

Table VI
Distribution of malnutrition regarding primary health condition

Primary health condition	(B + C) score ^s
Hematological diseases	69.7
Chronic liver disease	67.2
Cancer	65.0
Chronic kidney disease	62.6
Respiratory diseases	58.9
Diabetes mellitus	38.5
Heart and blood vessels	35.6
Gastrointestinal diseases	34.3
Gynecological diseases	30.9
Urological diseases	25.3
Burns	25.0
Orthopedic and trauma illnesses	24.1
Neurological and psychiatric illnesses	21.6
Others	29.4
All problems	37.1

$\chi^2 = 393.99$; $p < 0.05$.

^sProportion of patients with (B + C) SGA scores for each health condition.

Size of the study serie: 5355.

Source: Records of the Ecuadorian ELAN Study of Hospital Malnutrition.

Records closed on: December 31th, 2012.

about by disruption of the functions tissues | organs | systems play in the economy.³⁶⁻³⁸

Malnutrition can also be an important comorbidity in other surgical clinical situations, as can be inferred from examining the relationships that might exist between nutritional status and health condition leading to admission. In this regard, malnutrition observed in (almost) one-quarter of the patients assisted for bone fractures, trauma and wounds caused by different types of weapons, as well in one-third of those with abdominal pain syndromes originated from cholecystitis, pancreatitis and appendicitis; is to be noticed.

Relationships between nutritional status and health status of the hospitalized patient as previously discussed might permeate other aspects of hospital manutrition. Malnutrition could be one the distinctive features of Internal Medicine services, occupied mostly by patients affected with non-communicable chronic diseases, and in whom organic chronic failure is prevalent; and the wards of General Surgery, on one hand, and Trauma, on the other; which concentrate patients evolving with major abdominal, orthopedic and trauma dramas, consuming prolonged lengths of hospital stay, and in whom infectious events such as pneumonia usually occur.

Malnutrition observed in Diabetes mellitus is not to be overlooked. The study revealed that 38.5% of the diabetic patients were malnourished, an estimate surpassing the one obtained for all-diseases. Diabetes mellitus has always been examined in the context of Obesity,³⁹⁻⁴⁰ but this association should not hide the

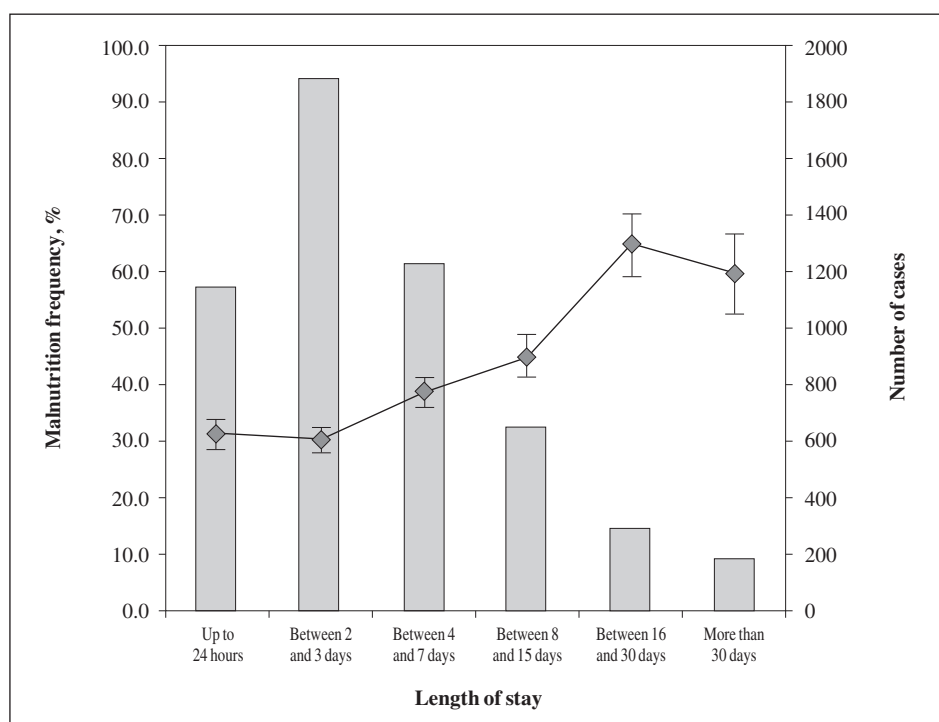


Fig. 3.— Influence of length of stay upon nutritional status. Estimated values of hospital malnutrition in each moment of hospitalization are shown, along with corresponding 95% confidence intervals.

increased risk of malnutrition diabetic patients are placed at due to complications resulting from diabetic microangiopathy such as kidney failure, peripheral arterial insufficiency and diabetic foot.⁴¹⁻⁴²

The influence of epi-biological factors upon hospital malnutrition could be estimated from the relationships existing between nutritional status and education level. Education level could be a subrogate of social and economical status of the subject within the community and society, as it has been previously pointed out.⁴³ Low education levels would imply incomes lower than the national average wage, and thus, inequities in the provision of medical care and/or difficulties in accessing foods and/or nutritional support therapies. On the other hand, education level would determine patient's capacity to assimilate knowledge and to incorporate skills allowing him/her to successfully deal with disease's metabolic and nutritional demands. In the case of the present study, it was striking that malnutrition concentrated among patients with grammar and junior high levels of instruction, as well as among those included within the "Undetermined" category, implying other interventions beyond those merely nutritional and medical would be required in order to ameliorate the existing nutritional disorders.

The cross-sectional design of the Ecuador ELAN Study withholds inferences that could be made about how hospitalization, and, by extension, the way medical care teams operate, affects nutritional status of the patient. Nonetheless, this study has been consistent with others⁴³⁻⁴⁵ in showing that malnutrition frequency increases as the patient accumulates more and more days of hospitalization, after adjusting the study series

for LOS. The hypothesis advanced by many authors that malnutrition is the distinctive feature of hospital populations with 16 (or more) days of admission is thus reinforced. Although the size of such populations could be artificially limited by means of an intense and rapid rotation of hospital beds, an elevated readmission rate would serve to signal those patients with a deteriorating nutritional status that are admitted again and again for the treatment of complications caused by a comorbidity that has not been identified and treated time- and convenient-ly.⁴⁶⁻⁴⁷

Clinical relevancy of the results of the present study

This study has presented the current state of malnutrition in public hospitals of Ecuador. As such, it represents the first organized, national-reaching effort to expose the magnitude of this co-morbidity. The study also extended to discuss possible determinants of hospital malnutrition after examining the influence of several selected demographic and clinical variables upon patient's nutritional status. In the current context, malnutrition seems to reflect opportunities lost by local medical care teams to address the metabolic and nutritional consequences of disease upon patient's health status, and thus, to conduct the required actions to identify, treat, and ultimately prevent malnutrition. It is abundantly documented the negative influence of malnutrition upon response to medical surgical treatment, quality and costs of medical care, and above all, the patient's own life. However, and in spite of such an

immense wealth of evidence, this study regrettably shows that hospital malnutrition is still a pending issue in the Latin American region.

Conclusions

Hospital malnutrition is an important health problem in public hospitals of the Republic of Ecuador. Further research could be oriented to the causes of this prevailing epidemiological phenomenon. In this regard, it would be interesting to explore the validity of a model previously described that sees hospital malnutrition as the result of failures in the availability of resources, failures in recognizing opportunities for nutritional intervention and/or absence of knowledge and skills in issues of clinical and hospital nutrition, nutritional support, artificial nutrition and metabolism.⁴⁸ Identification and removal of barriers that today still surround the implementation of coherent, cost-effective nutritional support schemes in the hospitalized patient would bring about containment of the costs of medical care, and a quality care better perceived by the patient and his/her relatives.⁴⁹

Epilogue

The completion of the Ecuadorian ELAN Study of Hospital Malnutrition has shown the maturity achieved by the School of Nutrition and Dietetics of the Faculty de Public Health at ESPOCH as a teaching and research institution that can successfully take on multicenter projects of national reach. This article thus becomes the best endorsement of the capacity of the School to satisfy other social commissions aimed to the continuous improvement of the quality of the health of the Ecuadorian people.

Composition of the Ecuadorian Group for the Study of Hospital Malnutrition

General Coordinator: Sylvia Gallegos Espinosa. *Scientific Advisor:* Marcelo Nicolalde Cifuentes. *International Advisor:* Sergio Santana Porbén. *Surveyors:* Janeth Ortega Urguilez: Hospital “Vicente Corral Moscoso” (Azuay); Paola Elizabeth Calle Barahona: Hospital IESS “José Carrasco Arteaga” (Azuay); Myriam Elizabeth Chavez Gavilanes: Hospital “Alfredo Noboa Montenegro” (Bolívar); Susana del Rocío Redrobán Dillón: Hospital IESS “Humberto del Pozo Santos” (Bolívar); María Eugenia Barrera Orellana: Hospital “Homero Castanier Crespo” (Cañar); Verónica Dayana Villavicencio: Hospital “Darío Machuca Palacios” (Cañar); Catalina Veronica Araujo Lopez: Hospital “Luis Gabriel Davila” (Carchi); Lorena Daniela Domínguez Brito: Hospital Central de Latacunga (Cotopaxi); María Victoria Padilla

Samaniego: Hospital Docente de Riobamba (Chimborazo); María Elena Lara Montenegro: Hospital IESS Riobamba (Chimborazo); John Sedamanos Cun: Hospital “Teófilo Davila” (El Oro); Mónica Beatriz Lucero Zuñiga: Hospital “Delfina Torres de Concha” (Esmeraldas); Carmen Elisa Naranjo Rodríguez: Hospital “Abel Gilbert Pontón” (Guayas); Angelica María Solis Manzano: Hospital Neumológico “Alfredo J Valenzuela” (Guayas); Mariana Jesus Gualla Paca: Hospital San Vicente de Paul (Imbabura); Diana Maribel Donoso Sánchez: Hospital IESS Manuel Ignacio Monteros (Loja); Tania Verónica Cabrera Parra: Hospital Regional “Isidro Cueva” (Loja); Cecilia del Carmen Méndez Arias: Hospital “Martín Icaza” (Los Ríos); Ruth Yaguachi Alarcón: Hospital IESS Babahoyo (Los Ríos); Edwin Geovanni Martínez Altamirano: Hospital Sagrado Corazón de Jesús (Los Ríos); Mariela del Carmen Ambi Ambi: Hospital “Nicolás Coto Infante” (Los Ríos); Lorena Patricia Yaulema Brito: Hospital “Rafael Rodríguez Zambrano” (Manabí); María de los Angeles Rodríguez Cevallos: Hospital IESS Manta (Manabí); José Vicente Mora Vera: Hospital “Verdi Ceballos Balda” (Manabí); Tania Valeria Carpo Arias: Hospital “Miguel H Alcivar” (Manabí); José Isaac Yumaglla Roma: Hospital de Macas (Morona Santiago); Marisol Costales Velastegui: Hospital “José María Velasco Ibarra” (Napo); Estefanía Morales Freire: Hospital “Francisco de Orellana” (Orellana); María Aide de la Cruz Calderón: Hospital de Puyo (Pastaza); José Ramírez Estévez: Hospital IESS Carlos Andrade Marin (Pichincha); María Cecilia Salazar Mera: Hospital “Eugenio Espejo” (Pichincha); María Lorena Silva Herrera: Hospital “Pablo Arturo Suárez” (Pichincha); Verónica Carlina Delgado López: Hospital “Gustavo Domínguez” (Santo Domingo de las Tsachilas); Silvia Elizabeth Bonilla Veloz: Hospital Nuestra Señora de la Merced (Tungurahua); Patricia del Carmen Flores Ortiz: Hospital Provincial Docente de Ambato (Tungurahua); Verónica Alejandra Jaya Baldeón: Hospital IESS Ambato (Tungurahua).

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Original / Otros

Interaction between mercury (Hg), arsenic (As) and selenium (Se) affects the activity of glutathione S-transferase in breast milk; possible relationship with fish and shellfish intake

Ramón Gaxiola-Robles^{1,2}, Vanessa Labrada-Martagón^{1,3}, Alfredo de Jesús Celis de la Rosa⁴, Baudilio Acosta-Vargas¹, Lía Celina Méndez-Rodríguez^{1,5} and Tania Zenteno-Savín¹

¹Centro de Investigaciones Biológicas del Noroeste, S.C. Instituto Politécnico Nacional 195, Playa Palo de Santa Rita Sur, La Paz, Baja California Sur, México. ²Hospital General de Zona No.1, Instituto Mexicano del Seguro Social, 5 de febrero y Héroes de la Independencia, Centro, La Paz Baja California Sur, México. ³Center for Stock Assessment Research, University of California Santa Cruz, Fisheries Ecology Division, Southwest Fisheries Science Center, NOAA, Santa Cruz, CA, USA. ⁴Departamento de Salud Pública, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Jalisco, Mexico. ⁵Valley Life Sciences Bldg, Museum of Vertebrate Zoology, University of California, Berkeley, CA, USA.

Abstract

Breast milk is regarded as an ideal source of nutrients for the growth and development of neonates, but it can also be a potential source of pollutants. Mothers can be exposed to different contaminants as a result of their lifestyle and environmental pollution. Mercury (Hg) and arsenic (As) could adversely affect the development of fetal and neonatal nervous system. Some fish and shellfish are rich in selenium (Se), an essential trace element that forms part of several enzymes related to the detoxification process, including glutathione S-transferase (GST). The goal of this study was to determine the interaction between Hg, As and Se and analyze its effect on the activity of GST in breast milk. Milk samples were collected from women between day 7 and 10 postpartum. The GST activity was determined spectrophotometrically; total Hg, As and Se concentrations were measured by atomic absorption spectrometry. To explain the possible association of Hg, As and Se concentrations with GST activity in breast milk, generalized linear models were constructed. The model explained 44% of the GST activity measured in breast milk. The GLM suggests that GST activity was positively correlated with Hg, As and Se concentrations. The activity of the enzyme was also explained by the frequency of consumption of marine fish and shellfish in the diet of the breastfeeding women.

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Key words: Breast milk. Generalized linear model. Glutathione S-transferase. Oxidative stress. Trace elements.

Correspondence: Lia Celina Méndez Rodríguez.
Centro de Investigaciones Biológicas del Noroeste, S.C.
Av. Instituto Politécnico Nacional.
Mar Bermejo 195. Col. Playa Palo de Santa Rita.
La Paz, B.C.S. Mexico.
E-mail: lmendez04@cibnor.mx

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EFFECTO DE LA INTERACCIÓN ENTRE MERCURIO (Hg), ARSÉNICO (As) Y SELENIO (Se) EN LA ACTIVIDAD DE GLUTATIÓN S-TRANSFERASA EN LECHE MATERNA; POTENCIAL RELACIÓN CON EL CONSUMO DE PESCADOS Y MARISCOS

Resumen

La leche materna es considerada como una fuente ideal de nutrientes para el crecimiento y el desarrollo de los recién nacidos, pero también puede ser una fuente potencial de contaminantes. Las madres pueden estar expuestas a diversos contaminantes como resultado de su estilo de vida y de la contaminación ambiental. Mercurio (Hg) y arsénico (As) pueden afectar negativamente el desarrollo del sistema nervioso fetal y neonatal. Algunos peces y mariscos son ricos en selenio (Se), un oligoelemento esencial que forma parte de diversas enzimas relacionadas con el proceso de desintoxicación, incluyendo glutatión S-transferasa (GST). El objetivo de este estudio fue determinar la interacción entre Hg, As y Se, así como analizar su efecto sobre la actividad de GST en la leche materna. Muestras de leche materna fueron obtenidas entre los días 7 y 10 después del parto. La actividad de la GST fue determinada espectrofotométricamente. Las concentraciones totales de Hg, As y Se fueron medidas por espectrometría de absorción atómica. Para explicar la posible asociación de las concentraciones de Hg, As y Se con la actividad de la GST en la leche materna, se construyeron modelos lineales generalizados. El modelo explicó el 44% de la actividad de GST medida en leche materna. El MLG sugiere que la actividad de GST se correlacionó positivamente con las concentraciones de Hg, As y Se. La actividad de la enzima se explica también por la frecuencia de consumo de peces marinos y mariscos en la dieta de las mujeres que se encuentran en periodo de lactancia.

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Palabras clave: Leche materna. Modelos lineales generalizados. Glutathione S-transferasa. Estrés oxidativo. Elementos traza.

Introduction

Humans are exposed to different contaminants as a result of their lifestyle and environmental pollution.¹ Trace elements, including mercury (Hg) and arsenic (As), are some of the most harmful xenobiotics because they are widespread and persistent in the environment.^{1,2} Selenium (Se), another trace element previously considered as toxic, is now known for its remarkable health benefits as an antioxidant, hormonal regulator, anti-carcinogenic properties, enhancer of immune surveillance, cell-cycle effector, enhancer of apoptosis and inhibitor of angiogenesis.³ Humans are exposed to Hg, As and Se from many sources.⁴ The most important sources include diet and drinking water.^{1,5,6} For some children the exposure starts *in utero* and continues during lactation.⁷ Hg, a naturally occurring heavy metal known to be toxic for humans, is of particular concern for the fetus and neonate given its negative effects on neurodevelopment.^{1,7} The toxicity of Hg strongly depends on its chemical form; elemental mercury (Hg⁰), inorganic (typically divalent, Hg⁺²) when combined with other elements, or in organic compounds when combined with carbon (*e.g.* methylmercury, MeHg⁺).¹ Both MeHg⁺ and Hg²⁺ are the most toxic due their high diffusion capacity through lipid membranes.¹ This process explains how Hg concentration can increase along the food web (marine ecosystems), a phenomenon referred to as biomagnification.^{6,8} The provisional tolerable weekly intake (PTWI) for total Hg is 5 µg/kg⁻¹ bw (body weight) week⁻¹ with no more than 1.6 µg/kg⁻¹ bw week⁻¹ of MeHg⁺, and some safe limits of Hg range from 0.001 mg kg⁻¹ to 1 mg kg⁻¹ depending on food or drink type.^{5,8-11}

The US Environmental Protection Agency¹⁰ has classified As as a known carcinogen (category A)³ associated with increased risk of cancer in the lung, skin, liver and bladder. Children that were exposed to As during early life or in-utero had marked increases in several chronic respiratory symptoms.¹² On the other hand, some studies suggest that As can be beneficial for animal growth and, in pharmacological amounts, As has been successfully used against some forms of leukemia.¹³ Humans are mainly exposed to As through diet and drinking water. Arsenic exists in four oxidation states, As(+V) (arsenate), As(+III) (arsenite), As⁰ (arsenic), and As(-III) (arsine). In addition to these forms, and their methylated derivatives, there are over 50 additional arsenic species identified in marine organisms, which show a wide range of toxicities, such as arsenocholine, arsenobetaine and arsenosugars and are considered innocuous to monomethyl (MMA) and dimethyl species (DMA) that are considered toxic.¹⁴ Arsenic toxicity assessment is more complex when the degree of toxicity is compared between inorganic and organic species: MMA(+III) > DMA (+III) > As(+III) > As(+V) > MMA(+V) > DMA(+V)¹⁵. Just like Hg, there are many thresholds cited in the literature as safe limits of As consumption. The provisional tolerable weekly intake (PTWI) of As for children is 15 µg/kg⁻¹

body weight per week, and safe limits of As are considered between 1 µg L⁻¹ and 25 µg L⁻¹ in breast milk and drinking water.^{10,16}

Prior to 1957, Se was considered a toxic element, but was subsequently recognized as an essential dietary trace element. Further, with the discovery of glutathione (GSH) and several other molecules that contain Se (selenoproteins), a biochemical function was assigned to this element.¹⁷ Se has many biological effects; in the human body, it plays a role as an antioxidant, participates in hormone metabolism, in redox reactions, in reproduction and immune function¹⁸. The levels of this element depend on its intake; it is present in meats, fish, shellfish and vegetables.¹⁷⁻¹⁹ A joint Food and Agriculture Organization/World Health Organization²⁰ expert committee on Human Vitamin and Mineral Requirements proposed a recommended minimal nutrient intake of 6 µg Se day⁻¹ in infants aged 0 to 6 months weighing approximately 6 kg.¹⁷

Metal detoxification is an essential process for all organisms.²¹ A number of mechanisms have been proposed to be involved in trace element detoxification. One of these is related to the selenoproteins, including glutathione S-transferase (GST) which has important antioxidant and detoxification functions.²¹ The superfamily of GST is associated to metal detoxification. Some xenobiotics, such as As and Hg, are metabolized by conjugation with GSH, a reaction catalyzed by the GST enzyme. Usually, conjugation with GSH is the first step in the detoxification process. Selenium is found as a central part of this process. Therefore, the GST enzyme and Se play an important role *in vivo* in the metal detoxification process.²²

The exposure to As and Hg presents important public health problems, especially for neonates when the possibility of contaminant transfer through breast milk is considered. Mothers are exposed to As and Hg by oral, inhalation and dermal routes. The oral route is considered to be the main exposure; therefore, a mother's nutrition during pregnancy and lactation period is very important. Fish and shellfish are rich sources of fatty acid and micronutrients such as Se, zinc and iron, especially in marine species. However, a diet rich in marine species may be regarded as a major pathway of exposure to contaminants including Hg and As.¹ Because a link between GST activity and Se concentration may participate in the detoxification process after exposure to Hg and As, the goal of this study was to determine the concentrations of [Se], [Hg] and [As], and evaluate its effect on the activity of GST measured in breast milk of women from Baja California Sur, Mexico.

Methods

Sampling

Breast milk samples were collected from women (*n* = 108) in Baja California Sur, Mexico. In the first

interview, informed consent was collected on the day of discharge from the hospital. In a second interview, 7 to 10 days after delivery, a survey was administered and milk samples were collected following the established sample collection procedure.²³ The study protocol adhered to the tenets of the Declaration of Helsinki and was approved by Capítulo Baja California Sur de la Academia Nacional Mexicana de Bioética, A.C. All samples were stored and frozen at -80 °C in Centro de Investigaciones Biológicas del Noroeste, S.C. until Hg, As, Se determinations and GST activity analyses were performed.

Exposure assessment

The time-frame explored for food consumption analysis was 30 days prior to breast milk sample collection. No information was obtained regarding portion size, recipes, or preparation methods. Fish and shellfish consumption frequency data were grouped into four categories; never consumed, consumed once a month, consumed once every two weeks and consumed more than twice a week.²³

Total concentration of mercury, arsenic and selenium analysis

Breast milk samples were transferred into Teflon vessels and digested with 70% nitric acid (HNO₃) and 30 % hydrogen peroxide (H₂O₂) in a microwave oven (Mars 5x, CEM, Matthew, NC, USA). Total concentration of Hg ([THg]), As ([TAs]) and Se ([TSe]) were quantified using a hydride system (HG 3000, GBC, Australia) coupled to an atomic absorption spectrophotometer (XplorAA, GBC, Braeside Australia). The cold vapor technique was used for [THg], and hydride generation for [TAs] and [TSe].²⁴ The detection limits (DL) were 0.05 µg L⁻¹ for Hg and 0.02 µg L⁻¹ for As. Analyses were performed in duplicate, including blanks; calibration standards and certified material (SRM1954 for Hg and GBW10017 for As and Se) of milk was included, with ≥ 90% recovery.

Activity of glutathione S-transferase (EC 2.5.1.18) analysis

GST activity was determined by measuring the change in absorbance caused by the formation of thioether glutathione dinitrobenzene complex as a product of the reaction between GSH and 1-chloro-2,4-dinitrobenzene (CDNB).²⁵ Working solution (0.1 M phosphate buffer, 10 mM GSH, and 60 mM EDTA), CDNB (10 mM) and the sample were mixed in a cuvette. Change in absorbance was recorded every 30 s during 6 min at 340 nm. Enzyme activity was expressed in units mg⁻¹ of protein (U mg⁻¹ protein). One unit of GST activity

is defined as the amount of enzyme that catalyzes the production of 1 mol of CDNB per min.

Statistic analyses

Descriptive statistics were calculated, including means, medians, minimum, maximum, 10th and 90th percentiles, as well as the proportion of the values below the DL. In those cases in which the values were below the DL, a value corresponding to half the DL was used for statistical analysis²⁶. GST activity, [TSe], [THg] and [TAs] values were not normally distributed (Kolmogorov-Smirnov $p < 0.01$). Therefore, non-parametric statistics (Kruskal-Wallis for four groups) were performed to evaluate differences in trace element concentration and GST activity between frequency categories of fish and shellfish intake.

A generalized linear model (GLM) was performed considering a *Gamma* distribution error to explain the activity of GST measured (response variable) in breast milk, using a *log* canonical link function.^{27,28} The *Gamma* distribution can be used as an alternative of the *Gaussian* or *Poisson* distribution error for continuous positive data;^{28,29} it extends over the range of where is the value of the variable of interest (GST activity).³⁰ The applicability of this distribution lies in its flexibility, from an inverse curve or right-hand skewed curve (when the dispersion parameter, ν , is small relative to the μ^2) to a bell shaped and symmetric curve (for larger values of ν).^{28,30} The explanatory variables considered for modeling were [TSe], [THg], [TAs] and frequency categories of fish and shellfish intake; the former considered as factor variables included in the GLM. The simplification and selection of the minimal adequate model was performed starting with the maximal model containing all the factors, interactions and covariates of interest ($k = 31$ this study);³¹ the simplification was done using the backward procedure evaluating all the alternative models by testing the contribution of each variable in turn ($p < 0.05$), and the change in the residual deviance at each step.^{28,32} The deviance criterion is used as a measure of the goodness-of-fit of the model to the data.²⁸ Finally, the distribution of deviance residuals of the minimal-fitted model was evaluated as a diagnostic method and model validation.²⁸ Equations for the minimal-fitted models were generated in terms of the explanatory variables with significant contribution to GST activity.

Results

Total mercury, selenium and arsenic concentrations; GST activity

[THg], [TSe] and [TAs] concentrations and the GST activity were measured in breast milk of 108 women from Baja California Sur Mexico; results are summa-

Table I
Glutathione S-transferase (GST) activity (U mg⁻¹ protein) and trace element levels (μg L⁻¹) in breast milk of women inhabiting Baja California Sur, México

Variable	N	Minimum	Maximum	Mean	Median	P10	P90	% < LD*
GST U mg ⁻¹ prot	108	0.00001	0.070	0.007	0.002	0.0003	0.025	–
[THg] μg L ⁻¹	108	0.03	24.87	2.52	1.54	0.03	5.51	14%
[TSe] μg L ⁻¹	108	6.32	56.13	21.95	19.78	12.5	32.23	–
[TAs] μg L ⁻¹	108	0.01	13.80	0.99	0.01	0.01	4.99	76%

% < LD: Percentage of values under the detection limit; P10: Percentile 10th; P90: Percentile 90th; GST: Glutathione S-transferase; [THg]: Total mercury concentration; [TSe]: Total selenium concentration; [TAs]: Total arsenic concentration.

rized in table I. The median of [THg] was 1.54 μg L⁻¹ (range 0.03 to 24.87 μg L⁻¹); in 14% (15/108) of the samples the concentration was below the DL. In breast milk samples, the median [TSe] was 19.78 μg L⁻¹ (range 6.32 to 56.13 μg L⁻¹). For [TAs] a median of 0.99 μg L⁻¹ (range 0.01 to 13.80 μg L⁻¹) was found, with 76% (82/108) of the samples having concentrations below the DL. The median GST activity was 0.002 U mg⁻¹ protein (range 0.00001 to 0.07 U mg⁻¹ protein).

Trace element concentrations and GST activity by categories of intake

The median and percentiles (10 and 90%) of the continuous variables categorized by the frequency of intake for fish and shellfish are presented in table II. The group that never ate fish tends to present lower levels of [THg], [TSe] and GST activity compared with those who consumed fish more than twice a week; however, there was not a statistically significant difference associated to the frequency of fish and shellfish intake in the [THg], [TSe] ($p \geq 0.05$) nor GST activity in breast milk ($p \geq 0.05$). A significant difference in [TAs] was observed when the frequency categories of shellfish intake were evaluated ($p = 0.04$), with the higher levels of [TAs] found in women who never ate shellfish or ate it once a month (table II).

Relationship between trace elements and GST activity in breast milk

The variability in the GST activity measured in breast milk was explained in the GLM by the simultaneous effect of the frequency of fish and shellfish consumption, the concentration of [TSe], [THg] and [TAs], as well by the interaction between trace elements (table III). The minimal fitted model chosen with $k = 8$ covariates (GST activity ~ Intercept, [TSe], [THg], [TAs], shellfish and fish intake, [TSe] * [THg], [TSe] * [TAs], [THg] * [TAs]) presents a difference in residual deviance of 44% ($\beta = -7.528$, *Std Error* = 0.770, *residual deviance* = 193.27, $p < 0.01$, $k = 8$) in comparison with the residual deviance of the maximal model with $k = 31$ covariates ($\beta = -6.618$, *Std Error* =

1.7599, *residual deviance* = 96.426, $p < 0.01$, $k = 31$). The former means that by choosing only 8 covariates, statistically significant ($p < 0.05$), the variability in the activity of GST in breast milk was explained with greatest accuracy (fig. 1), in comparison with the variability explained (only 44% higher) by a maximal model with 31 covariates with no explicative power ($p \geq 0.05$). The equations for the fitted values of activity of GST are presented by categories of fish and shellfish frequency intake (table IV). The median values of the fitted data obtained by the model agreed in general terms with the median values of activity of GST observed (table IV). When the simultaneous effect of the eight covariates (frequency of intake of fish and shellfish, trace elements and the interaction between trace elements) are considered to explain the activity of the enzyme in breast milk, a tendency to increase of the GST activity is observed in the median fitted values together with the increase in the frequency of consumption of fish, with the lower values present in those women who never ate fish independently of their frequency of consumption of shellfish (table IV). The higher activity of GST fitted by the model are found in those women who consumed fish “once every two weeks” and “more than two times a week” together with the consumption of shellfish “once every two weeks” (table IV).

GST activity, trace elements and their regulatory thresholds

When the values of GST activity fitted by the model were plotted against the concentration of each trace element the majority of the values of the activity of the enzyme in breast milk were found under 0.02 U mg⁻¹ proteins (fig. 2). In all samples [TSe] was above 6 μg L⁻¹, which is the minimum recommended intake for infants fed with human milk established by the Joint FAO/WHO Committee (1998; fig. 2a).²⁰ The highest [TSe] was 56.1 μg L⁻¹, and only 1.8% (2/108) of the samples had levels up to 45 μg L⁻¹, which was set as tolerable upper intake for infants aged 0 to 6 months³³ (fig. 2a). The median concentration of [THg] in breast milk for those women who frequently consumed shellfish (3.22 μg L⁻¹) and fish (3.35 μg L⁻¹) (table II) is lower than the threshold marked by Agency for Toxic

Table II

Median of glutathione S-transferase activity (GST, U mg⁻¹ protein), total mercury ([THg]), total arsenic ([TAs]) and total selenium ([TSe]) concentration (μg L⁻¹) by fish and shellfish intake in breast milk of women inhabiting Baja California Sur, México

Frequency of intake	GST U mg ⁻¹ prot	P10	P90	*p	THg μg L ⁻¹	P10	P90	p	TSe μg L ⁻¹	P10	P90	p	TAs μg L ⁻¹	P10	P90	p
<i>Fish</i>																
Never	0.0019	0.00040	0.00758	>0.05	1.87	0.03	3.35	>0.05	18.84	10.14	31.59	>0.05	0.01	0.01	-	>0.05
Once a month	0.0010	0.00036	0.01617		1.10	0.03	5.40		19.86	11.87	36.10		0.01	0.01	5.04	
Once every two weeks	0.0033	0.00010	0.02872		1.43	0.03	5.67		19.72	9.39	31.85		0.01	0.01	5.63	
More than twice a week	0.0023	0.00030	0.01570		3.35	0.03	12.74		20.72	13.79	31.86		0.01	0.01	2.43	
<i>Shellfish</i>																
Never	0.0025	0.0002	0.0380	>0.05	1.10	0.03	3.71	>0.05	19.63	10.25	33.79	>0.05	0.01	0.01	5.3	0.04
Once a month	0.0019	0.0004	0.0089		1.53	0.03	6.81		18.25	11.60	31.08		0.01	0.01	6.25	
Once every two weeks	0.0022	0.0002	0.053		1.91	0.03	5.49		25.41	13.56	35.28		0.01	0.01	0.01	
More than twice a week	0.0019	0.0002	-		3.22	0.03	-		23.39	15.34	-		-	-	-	

*Statistical significance by Kruskal-Wallis. P10: Percentile 10th; GST: Glutathione S-transferase; [THg]: Total mercury concentration; [TSe]: Total selenium concentration; [TAs]: Total arsenic concentration.

Substances and Disease Registry¹⁰ (4 μg L⁻¹) and by Deutsche Forschungsgemeinschaft (5 μg L⁻¹) (fig. 2b).³⁴ By plotting the fitted values of the GST activity with [THg] is possible to show that [THg] in breast milk did not present values above 5 μg L⁻¹ (fig. 2b). The [TAs] in 81.5% (88/108) of the samples was under 1 μg L⁻¹, in accordance with the recommendation by ATSDR (2007) for breast milk, and in 1.8% (2/108) of the samples was 10 μg L⁻¹, which is considered as a safe limit for drinking water by WHO³⁵ (fig. 2c).

Discussion

In this study, the GLM, a multivariate statistical analysis, helps to explain the activity of the GST measured in breast milk of women from Baja California Sur by the evaluation of the simultaneous contribution of many covariates, including the interaction between trace elements. The *Gamma* distribution error chosen during the GLM analysis resulted very useful to evaluate the activity of the GST due to its large coefficient of variation and the condition of the variable skewed to the right. Using *Gamma* distribution error avoided the issue of negative values being generated, which results unrealistic when the variable of interest is continuous, positive and has a large variability.²⁹

Marine diet intake and trace element exposure

The minimal model chosen in this study explained the activity of GST by the simultaneous effect of the frequency of fish and shellfish consumption together with the concentration of [TSe], [THg] and [TAs], and also by the interactions between trace elements. Shellfish consumption did not have a significant contribution when the four categories were grouped ($p = 0.11$); however, shellfish consumed “once every two weeks” did contribute significantly ($p = 0.03$), generating the highest fitted values of GST activity together with the consumption of fish when consumed more than once every two weeks. With respect to the frequency of fish intake, the “never consumed” category presented statistically significant contribution in explaining the activity of GST, generating the lowest fitted values. However, there was not a direct effect of the frequency of intake of marine products over the GST activity of the women, when univariate analyses were performed (table II).

Fish is considered one of the main sources of Hg. Studies that included breast milk from women with high fish intake reported [THg] of 1.22 μg L⁻¹ to 4.1 μg L⁻¹.³⁶ WHO (1990), considers concentration ranges of 1.4 to 1.7 ng Hg g⁻¹ as ‘normal’ in breast milk. The results from the bivariate analyses of this study did not show a clear pattern between [THg] in breast milk and the frequency of intake of fish and shellfish among women in Baja California Sur (table II), even when

Table III
Coefficients fitted by the generalized linear model (GLM) with Gamma error distribution for glutathione S-transferase (GST) activity (U mg⁻¹ protein) in breast milk of women inhabiting Baja California Sur, México

Model	Variable	Unstandardized coefficients		z	p	Deviance (df)		Scaled deviance (df)		95% Confidence interval of b	
		b	Std. Error			minimal	model	minimal	model	Lower	Upper
GST	(Intercept)	-7.528	0.770	-9.777	<0.01	193.27(95)		95(95)		-9.068	-5.988
	[TSe]	0.061	0.021	2.919	<0.01					0.019	0.103
	[THg]	0.772	0.169	4.557	<0.01					0.433	1.111
	[TAs]	0.369	0.116	3.174	<0.01					0.136	0.602
	[TSe] * [THg]	-0.029	0.006	-4.515	<0.01					-0.042	-0.016
	[TSe] * [TAs]	-0.015	0.005	-3.170	<0.01					-0.025	-0.006
	[THg] * [TAs]	-0.003	0.023	-0.112	0.91					-0.076	0.018
	Shellfish never consumed	0.857	0.446	1.923	0.05					-0.034	1.748
	Shellfish consumed once a month	0.332	0.427	0.777	0.44					-0.522	1.185
	Shellfish consumed once every two weeks	1.195	0.565	2.115	0.03					0.065	2.326
	Shellfish consumed more than twice a week	0 ^a	-	-	-						
	Fish never consumed	-1.036	0.494	-2.100	0.04					-2.024	-0.049
	Fish consumed once a month	-0.163	0.504	-0.322	0.75					-1.171	0.846
	Fish consumed once every two weeks	0.221	0.509	0.434	0.66					-0.798	1.240
	Fish consumed more than twice a week	0 ^a	-	-	-						

^aSet to zero because this parameter is redundant. GST: Glutathione S-transferase; Std. Error: Standard error; df: degrees of freedom; [THg]: Total mercury concentration; [TSe]: Total selenium concentration; [TAs]: Total arsenic concentration.

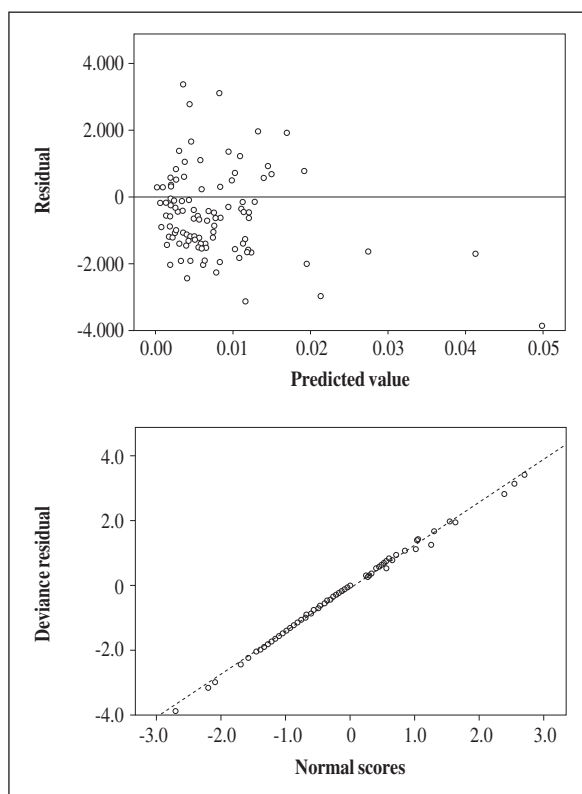


Fig. 1.—Residual plots of the minimal adequate model for glutathione S-transferase (GST) activity in breast milk of women inhabiting Baja California Sur, Mexico.

[THg] of up to $1.69 \pm 0.18 \mu\text{g g}^{-1}$ and 0.01 to $0.51 \mu\text{g g}^{-1}$ have been reported, respectively, in muscle of blue shark and yellowfin tuna, both locally caught and consumed.^{19,37} In this study, [TAs] was below the DL in 76% of the samples, under the concentration ($1 \mu\text{g L}^{-1}$) established by ATSDR (2007) as the safe limit for breast milk in 82% of the samples, and close to or above the threshold ($10 \mu\text{g L}^{-1}$) established as the safe limit for consumption of drinking water by WHO³⁵ in 2.7% of the samples. However, all samples were under the safe limit of $25 \mu\text{g L}^{-1}$ established in Mexico for drinking water¹⁶. In some areas of the world, drinking water may contain elevated [As]. Little As is excreted in breast milk, even in women with high exposure from drinking water. For example, in Argentina, around the Andes area, women are exposed to [As] of about $200 \mu\text{g L}^{-1}$ in drinking water, but their breast milk has approximately $2.3 \mu\text{g As L}^{-1}$.³⁸ If babies were given formula with local water, arsenic exposure could be 87 times higher than for infants fed with breast milk. Therefore, exclusive breastfeeding protects infants from potential As exposure in the water used to reconstitute formula.³⁹ The frequency of fish intake did not show any effect on the [TAs] in this study. Statistically, there is an association between [TAs] and shellfish intake; however, a biological explanation is confounded by high variability in the data (table I), lack of information for the category of frequency of shellfish intake

“more than twice a week”, and values below the DL for the group with shellfish intake of “once every two weeks” (table II). Therefore, the apparent association found in this study between dietary habits and [TAs] could only be applicable to those women who rarely (once a month) or never eat shellfish.

The concentration of [TSe] in all breast milk samples at 7 to 10 days postpartum (transition milk) in this study was above the threshold for minimal adequate ($6 \mu\text{g L}^{-1}$) intake for infants who were exclusively and freely fed human milk.^{17,18,20} Only 1.8% (2/108) of the samples showed [TSe] above the tolerable intake ($45 \mu\text{g L}^{-1}$).³³ The mean [TSe] in this study ($21.9 \mu\text{g L}^{-1}$) is 46% higher than the average recommended by the US Institute of Medicine for infants fed mainly with human milk ($15 \mu\text{g L}^{-1}$).⁴⁰ Both, geological factors and dietary habits, can be reflected in the elevated [TSe] found in breast milk in this study.

When the fish and shellfish intake frequency is considered, no association with [TSe] is observed ($p > 0.05$). However, [TSe] was 18% higher in those whose shellfish intake is more than twice a week as compared to those who never eat shellfish; similarly, [TSe] was 12% higher in those whose fish intake is more than twice a week as compared to those who never eat fish. The [Se] content in food can be extremely variable, depending on the combination of geological/environmental factors. The food items that are rich in [Se] are several species of fish and shellfish, approximately 1.5 to 6 times higher than in meats.¹⁸ The geological factors and conditions make Baja California Sur a [Se]-rich area.⁴¹ For example, [TSe] of $0.20 \mu\text{g g}^{-1}$ and $1.01 \mu\text{g g}^{-1}$ was recently reported in meat of yellowfin tuna, a fish species found in the coast of Baja California that is used for local consumption.¹⁹

Trace elements interactions and GST activity

The present study was conducted with the objective of analyzing the potential link between GST activity and Se in the detoxification process following exposure to Hg and As. The GST activity was explained in the GLM chosen by the concentration of [TSe], [THg] and [TAs] together with the interactions between trace elements, specifically the interaction between [TSe] with [THg], [TSe] with [TAs] and [THg] with [TAs] additionally to the frequency of fish and shellfish intake. The interactions between [TSe] with [THg] and [TAs] appear to have an antagonistic effect, reducing GST activity (tables III and IV). The antagonistic effect of the interaction between [THg] and [TAs] did not show a statistically significant contribution in the model ($p = 0.91$) that helps to explain the activity of GST; even so, it contributed to explaining the variability of the adjusted model. The former results can be explained by the metal detoxification role of GST.

Some xenobiotics, such as As and Hg are metabolized by conjugation with glutathione (GSH), a reac-

Table IV Fitted models for glutathione S-transferase activity and the total mercury (THg), selenium (TSe) and arsenic (TAs) concentration (μL ⁻¹) in breast milk of women inhabiting Baja California Sur, Mexico, with fish and shellfish intake					
Variable	Shellfish intake	Fish intake	Model	Median GST measured	Median GST fitted model
GST	Never	Never	$GST = e^{-7.707 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	0.0020	0.0028
		Once in a month	$GST = e^{-6.833 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	0.0010	0.0049
		Once e/2 weeks	$GST = e^{-6.430 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	0.0070	0.0089
		> 2 times in a week	$GST = e^{-6.671 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	ND	ND
	Once in a month	Never	$GST = e^{-8.233 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	0.0012	0.0014
		Once in a month	$GST = e^{-7.339 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	0.0001	0.0028
		Once e/2 weeks	$GST = e^{-6.976 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	0.0029	0.0048
		> 2 times in a week	$GST = e^{-7.196 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	0.0043	0.0059
	Once e/2 weeks	Never	$GST = e^{-7.369 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	0.0021	0.0022
		Once in a month	$GST = e^{-6.595 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	ND	ND
		Once e/2 weeks	$GST = e^{-6.112 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	0.0036	0.0118
		> 2 times in a week	$GST = e^{-6.333 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	0.0018	0.0120
	> 2 times in a week	Never	$GST = e^{-8.584 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	ND	ND
		Once in a month	$GST = e^{-7.690 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	0.0028	0.0020
		Once e/2 weeks	$GST = e^{-7.307 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	0.0015	0.0060
		> 2 times in a week	$GST = e^{-7.137 + 0.061 [TSe] + 0.772 [THg] + 0.369 [TAs] - 0.029 [TSe \cdot THg] - 0.015 [TSe \cdot TAs]}$	0.0011	0.0023

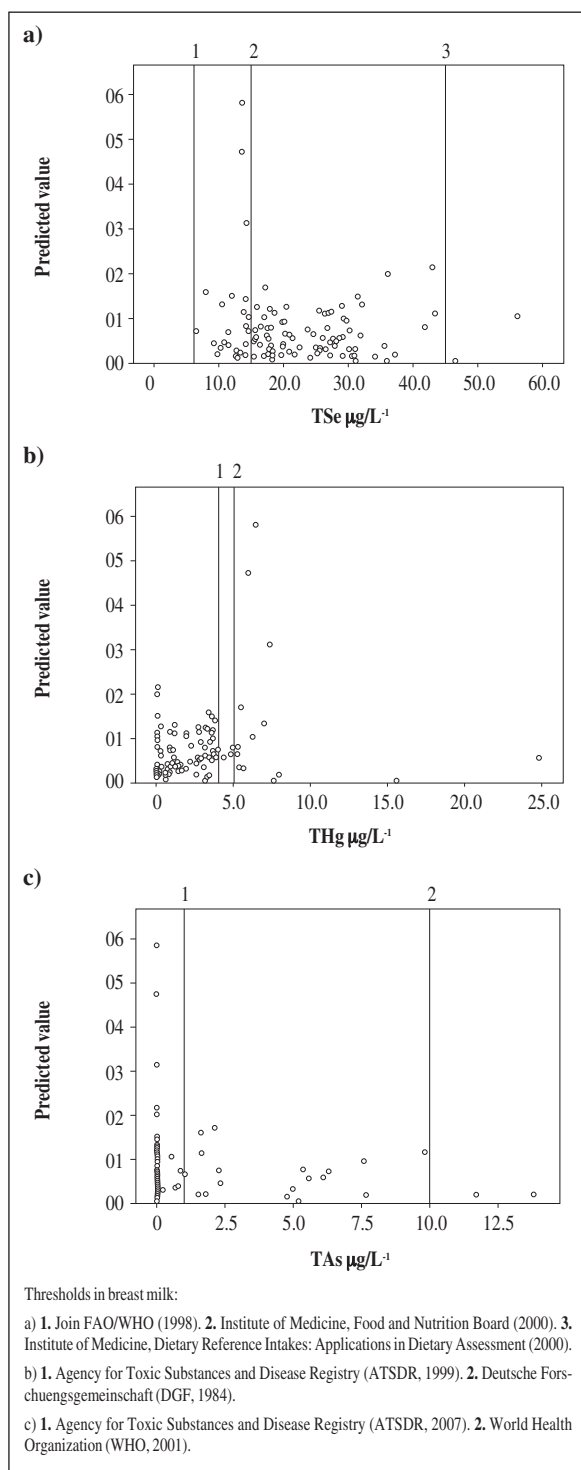


Fig. 2.—Relationship between fitted values of glutathione S-transferase (GST) activity and total concentration of a) selenium [TSe]; b) mercury [THg]; and c) arsenic [TAs] in breast milk of women inhabiting Baja California Sur, Mexico.

tion catalyzed by GST, and is usually the first step in the detoxification process. Selenium is a central part of this process; e.g., SeO_3^{2-} reacts with GSH to form a mixed disulphide, $2 \text{H}^+ + 4 \text{GSH} + \text{SeO}_3^{2-} \rightarrow \text{GSSG} + \text{GSSeSG} + 3 \text{H}_2\text{O}$.²² The main effect of trace elements,

such as Hg and As, with high affinity for the thiol groups (SH) of proteins and enzymes that are crucial in cell metabolism, is the production of reactive oxygen species (ROS), such as superoxide radical anion ($\text{O}_2^{\bullet-}$). The reaction with GSH can metabolize $\text{O}_2^{\bullet-}$ to protect cells from ROS-induced oxidative injury.²²

The role of Se against organic or inorganic Hg may be different. It is possible that Se interferes with the metabolism of inorganic Hg by reacting with Hg^0 to form a less toxic compound.⁴² The results from this study are in accordance with previous studies in which Hg accumulation is reduced in the presence of Se, while Hg accumulates to higher concentrations in the absence of Se.⁴³ This interaction between Se and Hg could be explained by the formation of a non-toxic Se-Hg complex with selenoprotein P, as was found in rat liver.⁴⁴ Although in this study only [THg] in breast milk was quantified and, thus, the fraction of it that corresponds to HgMe^+ is uncertain, the degradation of MeHg^+ to an inorganic form may be another protective mechanism that involves Se. When MeHg^+ is degraded to inorganic Hg, the methyl moiety can also be further degraded by homolysis to a methyl free radical.⁴² These molecules may initiate a chain reaction of peroxidation of various lipid constituents; at this point, the reaction with GSH catalyzed by GST contributes to avoidance of oxidative damage induced by the methyl free radical to different organic structures.²²

The formation of methylated metabolites is a critical step in the metabolism of inorganic and organic forms of Se and As, and it is generally assumed that the methylation pathway is directly related to the detoxification process (phase I and II). The metabolism and methylation of Se and As, are closely linked for the availability of GSH. As previously stated, inorganic forms of SeO_4^{2-} and SeO_3^{2-} are reduced by GSH to yield selenodiglutathione (GSSeSG) which is converted to hydrogen selenite (H_2Se). H_2Se is an intermediary metabolite for the synthesis of selenocysteine, which is further metabolized to the trimethylselenonium cation, the major urinary product of Se metabolism.³ Similarly, As^{5+} is reduced to As^{3+} by arsenate reductase or purine nucleoside phosphorylase (PNP), which requires GSH;⁴⁵ subsequent methylation by As methyltransferase generates di- and trimethylated metabolites with the same excretion route as Se^3 .

Other studies have described a direct interaction between Se and As^{46} in aqueous solution (in the present study, milk) which may play a role in dissolution of these elements.³ Many chemical forms of Se have been described in nature. In the diet, Se occurs in the +6 oxidation state as selenate (SeO_4^{2-}), +4 oxidation state as selenite (SeO_3^{2-}), 0 oxidation state as elemental (Se), -1 oxidation state as selenocystine, and -2 oxidation state as selenocysteine.³ Similarly, As can occur in the As^{5+} oxidation state as arsenate, As^{3+} oxidation state as arsenite, 0 oxidation state as elemental As, and the -1 and -2 oxidation as arsenical pyrites.³ Because Se and As have similar chemical and physical properties (e.g.

similar valance shell, electronic structure and atomic radio) they can be biologically antagonist to each other reducing their potential toxicity.

All previous alternatives can contribute to explain the finding in this study, that the GST activity in breast milk samples appears to be reduced according to the negative correlations found between the activity of the enzyme and the [TSe] * [TAs] and [TSe] * [THg] interactions suggested in the proposed model. Nevertheless, neither Se-Hg nor Se-As complexes were quantified in the present study. The GST activity was also explained in this study by positive correlations with concentrations of [THg], [TAs] and [TSe] and to fish and shellfish intake. These results suggest that a diet which includes fish and shellfish (rich in Hg and Se)¹⁹ increases GST activity in breast milk, while the concentration of Se, interacting with Hg and As, has an antagonistic and protective effect reducing GST activity measured in breast milk.

Conclusion

The GST activity in human milk obtained from 108 breastfeeding women from Baja California Sur was positively correlated to [THg], [TAs] and [TSe], and the activity of the enzyme was also explained in the GLM by the frequency of consumption of marine fish and shellfish in the diet of the sampled women. Further, the generalized model constructed with the data from this study suggests that GST activity in breast milk samples is reduced by the interactions between [TSe] * [TAs], [TSe] * [THg] and [TAs] * [THg]. Potential interactions between these elements, speciation of each element, as well as the potential role of GSH and other antioxidants and their relative contribution to reduce the levels of xenobiotics in human milk warrant attention. Finally, the present study highlights the benefits of a marine fish and shellfish-based diet (rich in Se) during breastfeeding and enhances the notion that a marine diet should not represent a risk for neonates.

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Original / Otros

Política nutricional activa en la implementación del soporte nutricional hospitalario; resultados de un estudio observacional

Julia Rodriguez Bugueiro, Natalia Lacquaniti, María Cecilia Merkel y Anabel Villagra

Servicio de Nutrición. Hospital de Alta Complejidad en Red "El Cruce" Dr. Néstor C. Kirchner. Florencio Varela. Buenos Aires. República Argentina.

Resumen

Introducción: La desnutrición hospitalaria es responsable de altos índices de morbilidad y mortalidad. El objetivo del estudio es describir los resultados de la realización de un programa nutricional hospitalario para la implementación oportuna del soporte nutricional.

Métodos: El diseño fue observacional, prospectivo, unicéntrico. Se registraron todos los pacientes adultos ingresados en forma consecutiva a nuestro hospital durante el período enero 2012-septiembre 2013. La implementación del programa nutricional constó de: evaluación nutricional al ingreso; reconocimiento del paciente con indicación de iniciar soporte nutricional; implementación del mismo; monitoreo y seguimiento.

Resultados: Ingresaron 1268 pacientes. Se realizó evaluación nutricional por Evaluación Global Subjetiva a 1234 pacientes (97,3%). Se identificaron 821 pacientes (66,5%) con categoría A, 280 pacientes (22,7%) con categoría B, y 60 pacientes (4,9%) con categoría C. Presentaron indicación de soporte nutricional 269 pacientes (21,8%), de los cuales 227 (84,4%) lo recibieron. De los 340 pacientes (27,6%) que representan la desnutrición global del hospital (categorías B + C), un total de 219 pacientes (64,4%) presentaron indicación de comenzar con algún tipo de soporte nutricional, iniciando el mismo 181 pacientes (82,6%). De los 38 pacientes (17,3%) que no lo iniciaron, 28 pacientes (73,7%) presentaron EGS C, siendo el pronóstico ominoso del paciente el motivo principal de no inicio del SN.

Conclusión: La aplicación de un programa para la implementación oportuna del soporte nutricional permitió la evaluación nutricional de un elevado porcentaje de pacientes internados y la correcta utilización del soporte nutricional en una alta proporción de los mismos.

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Palabras clave: Soporte nutricional. Valoración nutricional. Terapia nutricional. Desnutrición.

Correspondencia: Julia Maria Rodríguez Bugueiro.
Servicio de Nutrición.

Hospital de Alta Complejidad en Red "El Cruce" Dr. Néstor C. Kirchner.
Av. Calchaquí 5401, Florencio Varela.
1888 Buenos Aires. Argentina.
E-mail: juliarodb@gmail.com

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ACTIVE NUTRITION POLICY IN THE IMPLEMENTATION OF THE HOSPITAL NUTRITIONAL SUPPORT; RESULTS OF AN OBSERVATIONAL STUDY

Abstract

Background: Malnutrition at hospitals is responsible for high morbidity and mortality** rates. This study aims at describing the results of the implementation of a hospital nutrition program with an eventual deployment of nutritional support.

Methods: Observational, prospective, single-centre design. All adult patients consecutively admitted in our hospital during the period January 2012-September 2013 were registered. The implementation of the nutrition program consisted of: nutritional assessment at admittance; examination of the patient with indications for starting nutritional support; implementation of nutritional support; monitoring and follow-up.

Results: 1,268 patients were admitted. 1,234 patients (97.3%) underwent a nutritional assessment by means of Subjective Global Assessment. 821 patients (66.5%) were identified with category A, 280 patients (22.7%) with category B, and 60 patients (4.9%) with category C. 269 patients (21.8%) presented indications for nutritional support of which 227 (84.4%) did receive it. A total of 219 patients (64.4%) out of the 340 patients (27.6%) representing the global figure of malnutrition at the hospital (categories B + C), presented indications for starting some kind of nutritional support. 181 patients (82.6%) initiated this nutritional support. 28 patients (73.7%) out of the 38 patients (17.3%) who did not initiate it showed EGS C, being the patients ominous prognostic the main reason for not starting the nutritional support.

Conclusion: The application of a program aimed at the eventual implementation of nutritional support allowed the nutritional assessment of a high percentage of inpatients and the correct use of nutritional support on a high percentage of these patients.

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Key words: Nutritional support. Nutritional assessment. Nutritional therapy. Malnutrition.

Abreviaturas

NE: Nutrición enteral.
NP: Nutrición Parenteral.
DN: Desnutrición.
SN: Soporte nutricional.
ELAN: Estudio Latinoamericano de Desnutrición.
EGS: Evaluación Global Subjetiva.

Introducción

Numerosas publicaciones científicas han demostrado que la desnutrición hospitalaria es responsable directa de mayores índices de morbilidad (cicatrización más lenta de heridas, aumento de la tasa de infección hospitalaria, mayor tiempo de hospitalización, etc.) y de un importante incremento en la mortalidad de los pacientes. Por el contrario, aquellos pacientes bien nutridos responden mejor a los diferentes tratamientos, transcurren con menores complicaciones post-operatorias y presentan una mejor evolución clínica logrando estancias hospitalarias más cortas. El reconocimiento del papel de la nutrición en el manejo integral del paciente hospitalizado ha dado lugar a un importante desarrollo en los últimos años en el campo de la nutrición artificial (la nutrición enteral (NE) y la nutrición parenteral (NP)), y es debido a que estas intervenciones nutricionales específicas pueden reducir el impacto negativo de la desnutrición (DN) que con frecuencia acompaña a las enfermedades crónicas y a los estados hipercatabólicos e hipermetabólicos de los pacientes internados¹⁻⁴. A pesar de ello, los estudios demuestran que las tasas de utilización de NE y NP, conocidas también como soporte nutricional (SN), en los hospitales son bajas, aún cuando la frecuencia de desnutrición hospitalaria encontrada es elevada⁵⁻⁷.

El Estudio Latinoamericano de Desnutrición (ELAN) fue un estudio multicéntrico realizado a través de la Federación Latinoamericana de Nutrición Enteral y Parenteral (FELANPE) en el año 2003, que involucró a 13 países con un total de 9346 pacientes, cuyo objetivo fue determinar la prevalencia de desnutrición hospitalaria medida por Evaluación Global Subjetiva (EGS). Dicho estudio mostró claramente la brecha existente entre la alta prevalencia de desnutrición hospitalaria encontrada y la baja frecuencia de uso del SN. La desnutrición hospitalaria fue del 50,2% (11,2% desnutridos graves y 39% desnutridos moderados) y el uso de SN fue del 7,9% (5,6% con NE y 2,3% con NP)⁸.

Entre las causas que favorecen esta situación podemos citar⁹⁻¹¹: falta de evaluación nutricional para identificar oportunamente los pacientes que se beneficiarían de dichas prácticas, falta de intervención activa para la implementación en tiempo y forma del SN, falta de conciencia por parte del equipo de salud sobre la importancia del estado nutricional del paciente en la evolución clínica de los enfermos, utilización de SN sólo en estados avanzados de enfermedad, falta de for-

mación adecuada por parte de médicos y nutricionistas sobre SN y falta de recursos económicos para la implementación del SN.

Reconocida la problemática actual, se desarrolló en nuestro hospital un Programa Nutricional desde el Servicio de Nutrición para contribuir a la disminución de la incidencia de desnutrición hospitalaria.

Objetivo

El objetivo de nuestro estudio fue analizar los resultados de la realización de un programa nutricional hospitalario para la implementación oportuna del soporte nutricional.

Métodos

El diseño del estudio fue observacional, prospectivo, unicéntrico. Se registraron todos los pacientes adultos ingresados en forma consecutiva a nuestro hospital durante el periodo enero 2012-septiembre 2013. Se excluyeron pacientes internados de los sectores de Admisión de Paciente Crítico (Emergencias), Hospital de día, Pediatría y Unidad de Terapia Intensiva Pediátrica.

El hospital es de alta complejidad y funciona en red con otros 6 hospitales de menor complejidad en la zona sur de la Provincia de Buenos Aires.

El Programa Nutricional constó de: Evaluación nutricional al ingreso, reconocimiento del paciente con indicación de iniciar SN, implementación del SN propiamente dicho y monitoreo y seguimiento del SN.

Evaluación nutricional

Se realizó a través de la EGS, que es un método clínico sistematizado y validado que, a través de un interrogatorio simple y un examen físico sencillo, logra obtener un diagnóstico subjetivo del estado nutricional del paciente. La aplicación de EGS permitió clasificar a los pacientes en 3 categorías: clase A bien nutrido; clase B DN leve-moderada o con sospecha de DN; y clase C severamente DN. Dicha valoración se realizó durante las primeras 48 hs. de internación, como establece la metodología¹².

En la práctica clínica, también se evaluaron pacientes a las 72 horas, principalmente en aquellos ingresados durante el fin de semana, por lo que fueron incluidos en el análisis. Aquellos pacientes evaluados más allá de las 72 horas fueron considerados como no evaluados.

Reconocimiento del paciente con indicación de iniciar SN

Las indicaciones de uso de NE fueron: pacientes normonutridos con complicaciones en la evolución clí-

nica que le impidan cubrir requerimientos nutricionales por vía oral exclusiva, pacientes con DN moderada que no cubran al menos 75% de sus requerimientos nutricionales por vía oral en un plazo igual o mayor a 3 días, pacientes con imposibilidad de ingerir alimentos por vía oral y pacientes con DN severa establecida.

Las indicaciones de uso de NP fueron: pacientes con imposibilidad de absorber nutrientes a través del tracto gastrointestinal y pacientes que no alcancen a cubrir requerimientos nutricionales por vía enteral y deban complementarse con NP.

Los pacientes con pronóstico ominoso inmediato, con internación prevista menor a 72 hs, o con negativa a la colocación de sonda de alimentación no fueron considerados para recibir SN.

Implementación del SN propiamente dicho

Previo a esta etapa, se comunicó al médico tratante la situación nutricional del paciente quien autorizó o no la implementación del SN.

En caso afirmativo, se realizó el cálculo de requerimientos nutricionales: Para soporte nutricional metabólico se estimó 25 a 30 kcal/kg/día, para mantenimiento de peso: 30-35 kcal/kg/día y para ganancia de peso: 35 a 40 kcal/kg/día.

Se utilizó peso actual ó actual estimado y, en caso de pacientes obesos, peso ideal.

Selección de fórmula y método de administración

Las fórmulas nutricionales de elección para adultos fueron fórmulas listas para usar. Para los pacientes críticos de terapia intensiva, se utilizaron fórmulas hiperproteicas con glutamina, excepto en pacientes con shock séptico e insuficiencia renal que se administró fórmulas poliméricas estándar al igual que para el resto de los pacientes internados. En el caso de ser pacientes con diabetes, se indicaron fórmulas específicas para diabéticos, y en pacientes con restricción hídrica, fórmulas hipercalóricas.

El método de administración fue por bomba de infusión continua por 24 hs.

Monitoreo y seguimiento diario del SN

En base a la tolerancia individual del paciente y al volumen de alimentación infundido en el día previo, se progresó la infusión de la misma hasta alcanzar requerimientos nutricionales estipulados.

Definiciones

Definimos SN a la implementación de NE y/o NP exclusivamente.

Tabla I
Características de la población

Variable	Mediana	ICC
Edad	49	32-59
	N	%
Sexo		
Femenino	568	44,8
Masculino	700	55,2
Categoría diagnóstica		
Cardiológica	42	3,3
Cirugía cabeza y cuello	71	5,6
Cirugía general	257	20,3
Traumatológica	133	10,5
Clínica	285	22,5
Neuroquirúrgica	283	22,3
Oncológica	197	15,5
Servicio de Internación		
Clínica médica	1002	79
Unidad de trasplante	20	1,6
Terapia intensiva de adultos	246	19,4

El uso de suplementos nutricionales orales fue relevado, sin considerarse SN.

Análisis estadístico

Las variables continuas fueron expresadas como media y desvío estándar o como mediana e intervalo intercuartilo de acuerdo a su distribución. Las variables categóricas fueron expresadas como números y porcentajes.

Se utilizaron tablas de contingencia para comparar variables categóricas.

El programa fue aprobado por el Comité de Ética y por el Comité Científico de nuestra institución. Los mismos consideraron que, por tratarse de una intervención habitual, no requirió consentimiento informado.

Resultados

Durante el período citado, ingresaron 1268 pacientes. Las características principales de la población se describen en la tabla I. En la figura 1, se describe el flujo de pacientes. Se realizó evaluación nutricional por EGS a 1.234 pacientes (97,3% de los ingresos), de los cuales 60 pacientes (4,8%) fueron evaluados con EGS a las 72 hs del ingreso. Se identificaron 821 pacientes (66,5 %) con EGS categoría A (bien nutridos), 280 pacientes (22,7%) categoría B (DN leve-moderada o sospecha de DN), y 60 pacientes (4,9%) con categoría C (DN severa). Un total de 73 pacientes (5,9%) no fueron aptos para contestar las preguntas con coherencia y fueron considerados evaluados no categorizados.

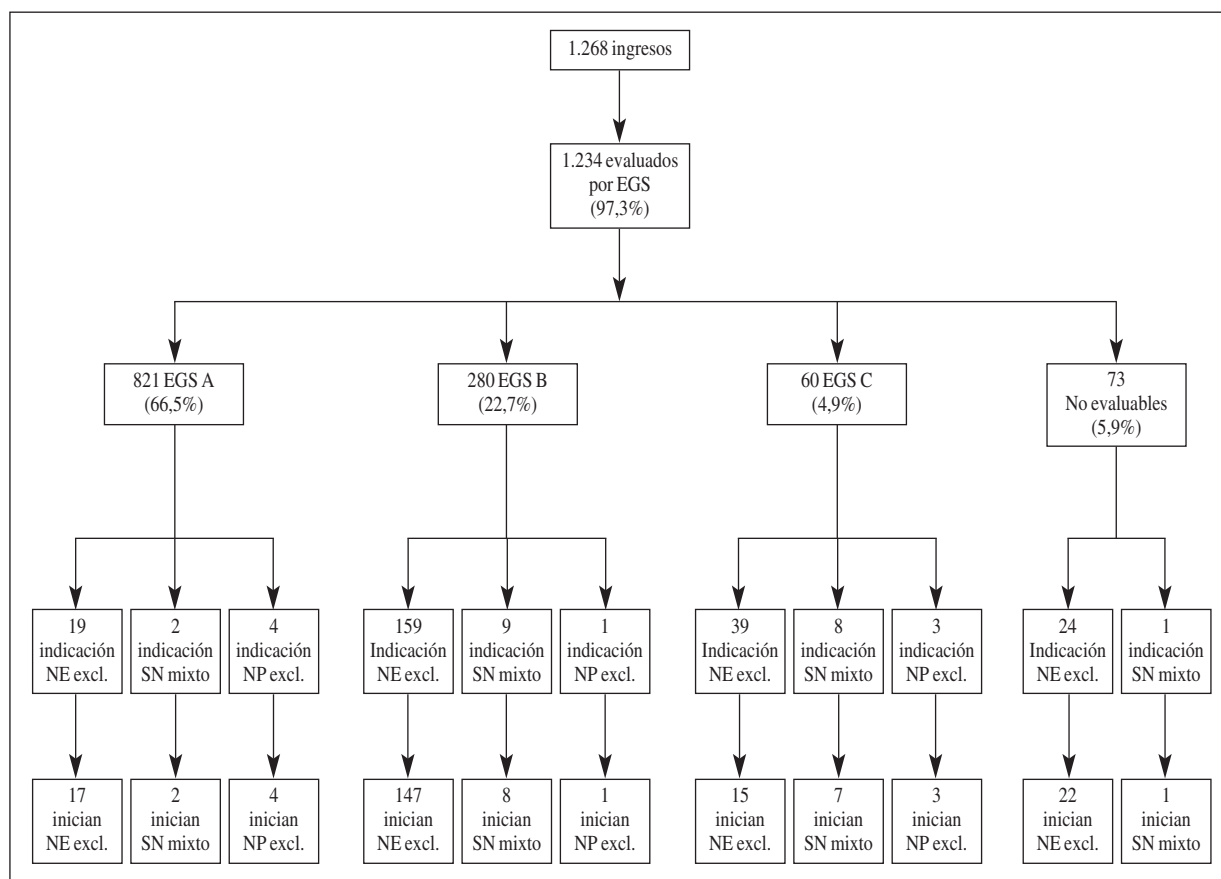


Fig. 1.—Flujo de pacientes.

Tabla II Resultados de la Evaluación Global Subjetiva			
EGS	N (%)	Indicación de SN	Inician SN
A	821 (66,5%)	25 pacientes (3%)	23 pacientes (92%)
B	280 (22,7%)	169 pacientes (60,3%)	156 pacientes (92,4%)
C	60 (4,9%)	50 pacientes (83,3%)	25 pacientes (50%)
No evaluable	73 (5,9%)	25 pacientes (34,24%)	23 pacientes (92%)
Total	1.234	269 pacientes (21,8%)	227 pacientes (84,4%)

EGS: Evaluación Global Subjetiva.

Tuvieron indicación de iniciar SN 269 pacientes (21,8%), de los cuales 227 (84,4%) lo recibieron (tabla II).

De los 340 pacientes (27,6%) que representan la DN global del hospital (EGS B + EGS C), un total de 219 pacientes (64,4%) presentaron indicación de comenzar con algún tipo de SN, iniciando el mismo 181 pacientes (82,6 %). De los 38 pacientes (17,3%) que no lo iniciaron, 28 pacientes (73,7%) presentaron EGS C, siendo

Tabla III Motivos de no inicio del SN en pacientes con EGS B + C	
Motivo de no inicio	N (%)
Pronóstico ominoso	16 pacientes (42%)
Alta temprana*	10 pacientes (26,3%)
Negativa del paciente al inicio del SN	6 pacientes (15,8%)
Negativa del equipo tratante al inicio del SN	5 pacientes (13,2%)
Óbito	1 paciente (2,7%)

SN: Soporte nutricional.

*Se considera alta temprana a aquella que se prevé menor a las 72 hs.

el pronóstico ominoso del paciente, el motivo principal de no inicio del SN (tabla III).

Entre los pacientes con indicación de iniciar SN, la chance de recibirla fue significativamente mayor entre aquellos con EGS A o B que con EGS C (OR 11,9; IC 95% 5,2 a 27,6; $p < 0,00001$).

En cuanto al uso de suplementos nutricionales orales, lo consumieron 103 pacientes (36,7%) con EGS B y 10 pacientes (16,6%) con EGS C.

Discusión

Hace 40 años, en 1974, Butterworth publicó el artículo “El esqueleto en el armario del hospital”¹³, con el obje-

tivo de llamar la atención acerca de las consecuencias que ocasiona la desnutrición hospitalaria en los pacientes. Detalló, además, una serie de prácticas responsables de la desnutrición, a las que denominó como “no deseables”: dilución de responsabilidades entre los miembros del equipo de salud, falla en reconocer la cantidad y calidad de la ingesta de los pacientes, indicaciones nutricionales deficientes, utilización del soporte nutricional en estados avanzados de desnutrición, falta de evaluación nutricional, entre otros. A pesar del tiempo transcurrido y de los artículos publicados sobre esta temática, la realidad en los hospitales no ha cambiado significativamente⁵⁻⁸.

En 1999, la Asociación Argentina de Nutrición Enteral y Parenteral (AANEP) realizó un estudio multicéntrico para conocer la prevalencia de desnutrición hospitalaria en diferentes regiones de Argentina. Dicho estudio mostró un 36,1% de pacientes con desnutrición moderada o riesgo de padecerla (EGS B) y un 11,2% de pacientes con desnutrición severa (EGS C), o sea, un 47,3% de prevalencia global de desnutrición, siendo el uso de soporte nutricional apenas del 9,3% (8,1% nutrición enteral y 1,2% de nutrición parenteral). El estudio de IBRANUTRI⁶ realizado en Brasil en el mismo año y el estudio ELAN CUBA⁷ realizado en el año 2003 mostraron resultados similares.

Aunque varios estudios previos han demostrado el impacto negativo que produce el estado nutricional deficiente en la morbilidad, mortalidad, días de internación y costos hospitalarios, en la práctica clínica sigue siendo baja la proporción de pacientes evaluados nutricionalmente, así como también el uso del soporte nutricional y, en muchos casos, es implementado sólo en estados avanzados de desnutrición¹⁴⁻²⁰.

Nuestros resultados demuestran una elevada proporción de pacientes evaluados nutricionalmente con EGS dentro de las primeras 72 hs. de internación, hecho que consideramos fundamental para poder lograr una alta proporción de utilización de SN en pacientes con DN establecida (EGS C) o en riesgo de padecerla (EGS B) y para que el soporte nutricional sea implementado de manera oportuna. La evaluación del estado nutricional del paciente internado fue precoz, adecuada y casi universal, y esto permitió un tratamiento amplio, focalizado principalmente en los pacientes con mayor beneficio potencial (frecuentemente EGS A y B), seleccionando una conducta conservadora más comúnmente en pacientes terminales o con patologías muy avanzadas (frecuentemente EGS C). Como se puede observar en la tabla II, el 83% de los pacientes con DN severa (EGS C) tuvieron indicación de SN, iniciándose la terapia sólo en el 50% de los mismos. En este subgrupo, la utilización de SN fue significativamente menor y esto contrasta con la elevada proporción de pacientes que iniciaron SN en los grupos de EGS A y B. Evidentemente, la desnutrición severa es una condición que acompaña a los estadios de enfermedad avanzada y/o terminal en los cuales el potencial beneficio del SN es mucho menor que en otros escenarios clínicos más

favorables, y el beneficio del inicio del SN en estos pacientes debe ser ponderado en función de otras variables. Por ello, entendemos que la evaluación nutricional al ingreso es clave para detectar al paciente que se beneficie de un soporte nutricional realizado oportunamente, evitando así las complicaciones que genera una desnutrición ya instaurada. Otro factor que consideramos importante para obtener estos resultados fue la coordinación y el acuerdo logrado entre el equipo de nutricionistas y médicos, ya que sólo en un 13,2% de pacientes no se inició SN por negativa del equipo médico tratante.

A pesar de que existe información publicada referente a la prevalencia de desnutrición hospitalaria en diferentes países y grupos de pacientes²¹⁻²³, como también de métodos de evaluación nutricional^{12,24-27} y programas para la detección precoz del paciente con desnutrición²⁸, no encontramos en la bibliografía estudios que evalúen el resultado obtenido con la implementación de programas protocolizados de soporte nutricional, haciendo muy difícil la comparación con estudios previos. Consideramos que debería existir un cambio en el paradigma de la investigación en este tema, que logre reorientar la investigación científica y las publicaciones hacia la búsqueda de soluciones prácticas y concretas a esta problemática ya reconocida. En este sentido, cabe destacar que nuestro estudio no sólo muestra los resultados de la evaluación nutricional y la prevalencia de desnutrición hospitalaria, sino que también evidencia el flujograma de los resultados obtenidos de la aplicación de nuestro programa en cada paciente, mostrando así la eficiencia en el uso del soporte nutricional (fig. 1).

Nuestro estudio presenta una importante limitación que debemos mencionar. Al reportar prospectivamente el resultado del programa, no relevamos datos de pacientes internados previamente a la implementación del mismo, lo que nos hubiese permitido evaluar el impacto de la intervención.

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Original / Otros

Dietary restraint and subjective well-being in university students in Chile

Berta Schnettler¹, Horacio Miranda¹, José Sepúlveda², Ligia Orellana², Soledad Etchebarne³, Germán Lobos⁴, Marcos Mora⁵, Marianela Denegri⁶ and Klaus G. Grunert⁷

¹Departamento de Producción Agropecuaria. Facultad de Ciencias Agropecuarias y Forestales. Universidad de La Frontera. Temuco. Chile. ²Centro de Psicología Económica y del Consumo. Universidad de La Frontera. Temuco. Chile. ³Departamento de Administración. Facultad de Economía y Negocios. Universidad de Chile. Santiago. Chile. ⁴Escuela de Ingeniería Comercial. Facultad de Economía y Negocios. Universidad de Talca. Talca. Chile. ⁵Departamento de Economía Agraria. Facultad de Ciencias Agronómicas. Universidad de Chile. Santiago. Chile. ⁶Departamento de Psicología. Facultad de Educación. Ciencias Sociales y Humanidades. Universidad de La Frontera. Temuco. Chile. ⁷MAPP Centre for Research on Customer Relations in the Food Sector. Aarhus University. Aarhus. Denmark.

Abstract

Objective: To characterize university students typologies according to chronic food restriction, satisfaction with life and food consumption.

Materials and method: A questionnaire was applied on a non-probability sample of 369 male and female students from five Chilean universities. The questionnaire included: Revised Restraint Scale (RRS), Satisfaction with Life Scale (SWLS), Satisfaction with Food-related Life (SWFL) and the Health-related Quality of Life Index. The survey included food and drink consumption habits, weight and approximate height and sociodemographic variables.

Results: Two factors in the RRS were detected by exploratory factor analysis: Preoccupation with Diet (PD) and Weight fluctuations (WF). A confirmatory factor analysis validated the bifactor structure of the RRS with an acceptable adjustment kindness. The cluster analysis allowed a distinction of four typologies with a significant variation in PD, WF, SWLS and SWFL scoring, number of days with mental health problems, frequency of alcoholic drinks consumption, restraint on the consumption of certain foods, drinks and spices, consumption frequency of fruit out of the main meals and types. Typologies did not differ on their body mass index.

Conclusions: Both, students preoccupied with diet and those who are not, experience higher levels of satisfaction with life and with food. Lower levels of global life satisfaction and satisfaction with food are related with the fluctuations in weight.

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Key words: Food restraint. Satisfaction with life. Satisfaction with food. Mental health.

RESTRICCIÓN ALIMENTARIA Y BIENESTAR SUBJETIVO EN ESTUDIANTES UNIVERSITARIOS EN CHILE

Resumen

Objetivo: Caracterizar tipologías de estudiantes universitarios según restricción alimentaria crónica, satisfacción con la vida y con la alimentación.

Material y método: Se aplicó un cuestionario a una muestra no probabilística de 369 estudiantes de ambos géneros de cinco universidades de Chile. El cuestionario incluyó: Escala Revisada de Restricción Alimentaria (RRS), Satisfaction with Life Scale (SWLS), Satisfaction with Food-related Life (SWFL) y el Índice de Calidad de Vida relativo a la Salud. Se consultaron hábitos de consumo de alimentos y bebidas, peso y estatura aproximada y variables sociodemográficas.

Resultados: Mediante análisis factorial exploratorio se detectaron dos factores en la RRS: Preocupación por la Dieta (PD) y Fluctuaciones de Peso (FP). Mediante análisis factorial confirmatorio se validó la estructura bifactorial de la RRS con una aceptable bondad de ajuste. Mediante análisis clúster se distinguieron cuatro tipologías que difirieron significativamente en los puntajes de PD y FP, los puntajes de la SWLS y SWFL, número de días con problemas de salud mental, frecuencia de consumo de bebidas alcohólicas, restricción del consumo de algunos alimentos, bebidas y condimentos, frecuencia de consumo de fruta a deshora y género. Las tipologías no difirieron en su índice de masa corporal.

Conclusiones: Tanto los estudiantes que se preocupan por la dieta como los que no, experimentan mayores niveles satisfacción con la vida y con su alimentación. Menores niveles de satisfacción global y en el dominio de la alimentación se relacionan con las fluctuaciones de peso.

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Palabras clave: Restricción alimentaria. Satisfacción con la vida. Satisfacción con la alimentación. Salud mental.

Correspondence: Berta Schnettler Morales.
Universidad de La Frontera.
Casilla 54-D, Temuco, Chile.
E-mail: berta.schnettler@ufrontera.cl.

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Introduction

Attending university is especially significant for the youth because it entails high levels of demand, competition and expectations that increase stress.¹ This period is also critical for the development of eating habits. Some studies report a low caloric intake in university students,^{2,3} mostly observed in women,⁴ which probably relates to gender stereotypes.⁵ Other research indicates that many university students do not follow healthy diets,^{6,7} which causes an increase in weight, fat and body mass index (BMI)⁷. Although a certain amount of weight gain can be expected at this stage in life, students who gain weight, particularly large amounts, may experience this as a significant stressor and resort to unhealthy weight control behaviors to cope with it. In this regard, youth are at a particularly high risk for disturbed eating behaviours⁸ or abnormal practices associated with eating disorders (e.g. restraint, emotional, disinhibited, binge, and late-night snacking; weight, shape, and eating concerns; strict dieting; among others).¹

The notion of restrained eating was first introduced by Herman and Mack.⁹ Dietary restraint behavior implies conscious attempts to reduce food intake in order to control body weight,^{10,11} although this behavior is not clearly associated with lower body weight. While some data suggest that restraint may be a useful strategy to control body weight,^{11,12} others report that an excessive restriction may have a counterproductive effect and may eventually be followed by weight gain¹³. The intent to diet may be disrupted by certain events such as distress,^{9,14} access to pleasant foods, alcohol, and other factors that disrupt self-control.¹⁴ The Restraint Theory¹⁰ states that eating behavior is affected by a balance of forces, including physiological pressures to eat and a non-physiological, self-imposed resistance (i.e. restraint) to these pressures. The Restraint Theory has suggested that dietary restraint or dieting contributes to overeating and eating disorders.¹⁵

Some studies show that eating disorders in youth are related to poor psychological health¹⁶⁻¹⁹ and low levels of life satisfaction.^{16,17,20} Evidence also indicates that university students who have healthful eating habits have better emotional health, lower prevalence of overweight and obesity, and greater satisfaction with life.²¹ Life satisfaction is the cognitive component of subjective well-being, either overall or by specific domains, such as health, family²² and food, among others. Positive evaluations of life satisfaction are linked to happiness and the achievement of the "good life".²³ However, it seems that the relation between dietary restraint/weight gain and subjective well-being is different between men and women. Weight gain has been shown to be associated with greater well-being for men,¹³ meanwhile studies reported that only for female university students dieting was associated with lower life satisfaction.^{17,20}

Therefore, in this research we will develop a typology of university students from various regions in

Chile based on their dietary restraint behaviors, and characterize them by their level of satisfaction with life and their food-related life, their eating habits and other health-related aspects. Studies conducted in Chilean universities report a prevalence of overweight and obesity of approximately 30-40%.^{3,21} A previous study conducted with university students from Southern Chile indicates that the nutritional state of said students does not only relate to their life satisfaction but also to their satisfaction with food-related life.²¹ However, to our knowledge, there have been no attempts to study the relation between dietary restraint and satisfaction in the domain of food, even though recent research concludes that food is among the important domains of life which affect an individual's well-being.^{21,24} The dietary restraint behavior will be measured using the Revised Restraint Scale (RRS).¹⁰ Our research will show that the distinction of chronic dieters and non-dieters, typical of many previous applications of the RRS, is too simple, and that perceived weight fluctuation is more important for satisfaction with life than diet concern.

Materials and method

A convenience sample was made up of 369 students from five state universities located in different geographical areas of Chile (Universidad de Tarapacá-Arica, Universidad de Chile-Santiago, Universidad de Talca-Talca, Universidad de La Frontera-Temuco, Universidad de Magallanes-Punta Arenas). All participants were volunteers, with a mean age of 20.9 years (SD = 2.27); 46.3% were men and 53.7% women; 95.4% resided in an urban area. To detect differences in terms of advancement in the university program, the sample inclusion criteria were students enrolled in first or third year at any of the aforementioned universities.

The questionnaire applied included the following scales:

- RRS (Revised Restraint Scale). The first measure of dietary restraint was developed by Herman and Mack⁹ and was later revised to a 10-item scale by Herman and Polivy.¹⁰ Factor analysis studies report two subscales: "Diet Concern" (DC) which evaluates the tendency of a person to restrain their food intake and the fear to gain weight, and "Weight Fluctuations" (WF), which registers weight fluctuation. The scores provide a measure of chronic food restriction and are commonly used to classify individuals into chronic dieters and non-dieters (usually using the median of the scores). In this research, the Spanish version of the RRS was used, which has shown adequate levels of internal consistency for each subscale (Cronbach's DC = 0.78; WF = 0.70-0.71) in previous studies in Chile.^{25,26} However, as previous studies in Chile (and most other applications of the RRS) were based on female samples only, and as our own study includes

both males and females, we will conduct additional testing regarding the dimensionality and reliability of the RRS for a mixed gender sample.

– HRQOL-4 (Health-related quality of life index): developed by Hennessy et al.²⁷ consists of four items that explore the self-perception of health, recent physical health (physical illness and injuries), recent mental health (stress, depression and emotional issues) and recent limitations on activity (education, work or leisure). This study used the Spanish version of the HRQOL-4, which has shown a good level of internal consistency (Cronbach's $\alpha = 0.78$) in a previous study in Chile²¹.

– SWLS (Satisfaction with Life Scale): developed by Diener et al.²² is a scale consisting of 5 items grouped into a single factor to evaluate overall cognitive judgments about a person's own life ("In most ways my life is close to my ideal"; "The conditions of my life are excellent"; "I am satisfied with my life"; "So far I have gotten the important things I want in life"; "If I could live my life over, I would change almost nothing").

– SWFL (Satisfaction with Food-related Life Scale): proposed and tested by Grunert et al.²⁴ consists of five items grouped into a single dimension ("Food and meals are positive elements"; "I am generally pleased with my food"; "My life in relation to food and meals is close to ideal"; "With regard to food, the conditions of my life are excellent"; "Food and meals give me satisfaction in daily life").

On the SWLS and SWFL scales the respondents must indicate their degree of agreement with the statements using a 6-point Likert scale (1: disagree completely, 6: agree completely). This study used the Spanish versions of the SWLS and SWFL, which has shown good levels of internal consistency in previous studies in Chile.²¹

Students were also asked about the frequency of consumption of nine groups of foodstuffs and drinks categorized by the National Statistics Institute in the Surveys of Family Budgets. Then, they were asked whether they restrained the intake of certain foods, drinks and condiments, as well as their reasons to do so. They were also asked about the frequency of snacking between meals and the perceived importance of food for their well-being using a 6-point Likert scale (1: not important at all, 6: totally and completely important). Finally, their estimated weight and height were consulted in order to obtain their BMI (kg/m²).

The execution of the study was approved by the Ethics Committee of the Universidad de La Frontera. Prior to the survey, the questionnaire was pretested with 30 students from said university with similar characteristics. As no problems were detected in the pretest, no changes were required in the questionnaire. The survey was administered through an online survey program (QuestionPro Inc) in June and August 2013. The participants signed informed consent statements before responding.

To evaluate the psychometric properties of the RRS, an exploratory factor analysis (EFA) was used followed by a confirmatory factor analysis (CFA). The EFA was implemented using SPSS 16.0 and the CFA using LISREL 8.8. The parameters were estimated by robust maximum likelihood. A bifactorial structure was assumed to exist for RRS. The variance extracted by the indicator variables of the latent factors was calculated. This indicator measures the proportion of variance extracted by a latent factor with respect to the total variance of that factor, including the variances of the measurement error of the factor items.²⁸ The compound reliability or compound Cronbach was obtained by an adaptation of Fornell and Larcker's formula,²⁸ which calculates the proportion between the sum of the standardized factor loadings of the items of a factor (indicator variables) squared, and the same amount plus the error variances associated with the items. The convergent validity was found by inspecting the significance of the t values of the factor loadings for each factor. The discriminant validity was obtained by comparing the extracted variance against the correlation between two factors. This test compares the extracted variance for each of the factors analyzed with the square of the correlation between the factors. The extracted variance for the factors must be greater than the value of the correlation; if this condition is fulfilled, it may be concluded that discriminant validity exists between the factors.²⁸ A CFA model fits reasonably well if the goodness-of-fit index (GFI) and the adjusted goodness-of-fit index (AGFI) are greater than 0.90, and if the root mean square error of approximation (RMSEA) is lower than 0.08.²⁸

To distinguish student types on the basis of chronic dietary restraint, a cluster analysis (hierarchical conglomerates) was used, with linkage by Ward's method and the squared Euclidian distance as the measure of similarity between objects. This analysis was applied to the Z-scores resulting from the factor analysis of the RRS scale. The number of groups was obtained by the percentage change of the recomposed conglomeration coefficients. To describe the segments, Pearson's Chi² test was applied to the discrete variables and a one-factor analysis of variance for the continuous variables. Because Levene's test indicated non-homogenous variances, the averages of variables with significant differences ($P \leq 0.001$ or $P \leq 0.05$) were separated according to Dunnett's T3 test for multiple comparisons.

Results

Both the SWLS and the SWFL presented adequate levels of internal consistency (Cronbach's α : 0.876 and 0.791, respectively) and a single factor grouped the five items of each scale (explained variance: 67.9 and 54.9%, respectively). The average score for the SWLS was 22.02 (SD = 5.3) and for the SWFL 18.46 (SD =

Table I
Results of factor analysis of principal components for the RRS in university students from various regions of Chile, August 2013

Items	Component	
	Diet concern (DC)	Weight fluctuations (FP)
8. Do you have feelings of guilt after overeating?	0,837	0,129
1. How often are you dieting?	0,747	0,130
5. Would a weight fluctuation of 2.5 kilos affect the way you live your life?	0,736	0,001
7. Do you give too much time and thought to food?	0,713	0,196
4. In a typical week, how much does your weight fluctuate?	0,046	0,786
3. What is the maximum amount of weight gain (in kilos) within a week?	0,295	0,752
2. What is the maximum amount of weight (in kilos) you have ever lost within 1 month?	0,042	0,752
Variance explained by component (%)	34,3	24,5
Cumulative variance (%)	34,3	58,8
Cronbach's α per component	0,768	0,703

Extraction method: Principal components analysis, Rotation method: Varimax with Kaiser normalization. Rotation has converged in 3 iterations. Measure of sampling adequacy: Keiser-Meyer-Olkin (KMO) = 0.764. Bartlett's Test of Sphericity, approximate Chi-square = 580,897; $gl = 21$; $p = 0.000$. Note: the remaining item should qualified the following standards: the eigenvalues of each extracted factor should be more than 1.000; the factor loadings of each reserved item should be more than 0.40; each item should be only loaded on a single factor; each factor should include at least 3 items.

4.8), from a theoretical maximum score of 30. Cronbach's α for the HRQOL-4 was 0.76. According to the first question from the HRQOL-4, most students perceived their health as good (37.1%) or very good (32.5%). The average number of days with physical health problems in the last month was 4.7 (SD = 5.9), the average with mental health problems was 7.5 days (SD = 8.4) and the average number of days in which the students could not carry on their usual activities due to health problems was 2.8 (SD = 4.1).

Most of the students eat bread (74.0%), soft drinks (55.0%), milk and dairy products (44.4%) and vegetables (47.2%) on a daily basis; two or three times per week they eat cereals and pasta (57.5%) and meat (50.1%); fruit is consumed daily (20.3%) or two or three times per week (36.3%); and occasionally fish and seafood (50.7%) and alcoholic beverages (43.9%). The majority of participants do not restrict consumption of sugar (59.6%), pastries (68.0%), salt (59.6%), fried and fatty food (47.4%), pasta and rice (88.3%), red meat (80.5%) and alcohol (45.8%). Regarding snacking between meals, 35.8% reported doing it "sometimes" and 33.3% "almost always". These snacks were mostly sweets (26.7%), yogurt (29.7%) and fruit (44.1%). 31.2% and 39.6% of the sample considered that food issues are "important" and "very important" for their personal well-being, respectively. The average BMI of the sample was 23.44 kg/m² (SD = 3.3). The nutritional state of the participants was in the low weight range for 1.6% of the sample (BMI < 18.5), normal weight range for 71.5% (BMI 18.5-24.99), overweight for 22.8% (BMI $\geq$ 25) and obesity for 4.1% (BMI $\geq$ 30).

Using EFA, two dimensions were detected on the RRS: Diet Concern (DC) and Weight Fluctuations (WF) that grouped seven of the ten original items (table I). Item 6 was eliminated because it presented communality values below 0.4. Items 9 and 10 were eliminated because they did not load on a single factor.

This result contradicts research that found an acceptable goodness of fit for the RRS with all items, though most have been conducted on women.^{29,30} These results partially correspond to those obtained by Mak and Lai³¹ in a sample of adolescents of both genders in Hong Kong (DC: items 1, 5, 7, 8, and 9; WF: items 2, 3, and 4). Some of the previous studies on the subject report a deficient behavior of item 9 of the RRS,^{25,26} which was also observed in the present research. Such variations can be due to the cultural context in which the instrument is applied. However, as noted above most previous applications have been based on female samples, and gender composition can hence be an additional source of variation in the pattern of item loadings. For the remaining items in this study, the DC and WF subscales presented an acceptable level of internal consistency. The CFA performed with the seven items of the RRS meant that the bifactorial structure could be validated with an acceptable goodness-of-fit (RMSEA = 0.074, GFI = 0.93, AGFI = 0.91). The standardized factor loadings for the seven items were statistically significant; therefore, it may be concluded that there is convergent validity. Both subscales presented acceptable values of extracted variance (DC = 0.470, WF = 0.401). Both subscales presented acceptable values of compound Cronbach's alpha (DC = 0.570, WF = 0.501). The value of the squared correlation between DC and WF (0.37) was lower than the extracted variances of the subscales, which verifies the discriminant validity between the constructs studied (fig. 1). Using the median of the RRS (14) considering seven out of 10 original items, 54.2% of the sample classified as chronic dieter and 45.8% as non-dieter.

Using a cluster analysis, four student types were detected with significant differences in the Z-scores (table II) of the two components obtained from the RRS ($p \leq 0.001$). The types differed significantly in the scores of the SWLS, SWFL ($p \leq 0.05$) and number of

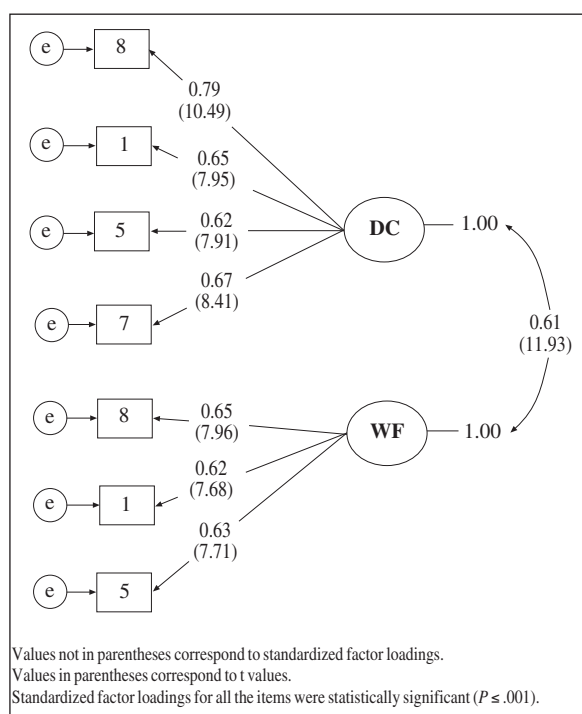


Fig. 1.—Confirmatory factor analysis established best-fitting model of RRS in an university student sample.

days with mental health problems ($p \leq 0.001$) (table III). They also differed in the importance assigned to food for personal well-being ($p \leq 0.05$), gender ($p \leq 0.001$) (table IV), restricted consumption of salt, alcohol ($p \leq 0.05$), pastries, fried and fatty food, pasta and rice and the frequency of consumption of alcoholic beverages ($p \leq 0.001$) (table V).

Group 1 “Satisfied with life, moderately satisfied with their food-related life, unconcerned about diet and weight fluctuations” (53.8%): participants in this group had a low score on the subscale DC, but it was significantly higher than Group 2’s score. They also presented a low score on the subscale WF but did not differ statistically from Group 4 in this regard (table II). Group 1 had the highest scores on the SWLS and SWFL but did not differ significantly from Group 4. This group reported the least number of days affected by mental health problems, but it did not differ from Group 2 (table III). It comprised a high proportion of students who think that food is “totally and completely important” for their well-being (11.6%) (table IV). There was a greater presence of students who did not restrict sugar consumption (71.2%), pastries (77.8%), fried and fatty foods (55.1%) and pasta and rice (94.4%).

Group 2 “Moderately satisfied with their lives and food-related life, concerned about weight fluctuations” (17.1%): this group scored significantly lower than the others in DC. The WF score was significantly higher than in Groups 1 and 4 (table II). The scores of the SWLS and SWFL were significantly lower than in Groups 1 and 4, but higher than in Group 3 (table III). This group was composed of a higher proportion of men (58.7%) and considers considered that food is “somewhat important” for their well-being (22.2%) (table IV). This group had a greater proportion of students that restricted the consumption of pasta and rice because they disliked it (4.8%), and of alcohol to prevent diseases (28.6%) (table V).

Group 3 “Moderately satisfied with life, dissatisfied with their food-related life, concerned about diet and

Table II						
Z score averages of groups obtained from cluster analysis, students of universities in Chile, August 2013						
Component	Group 1 (n = 198)	Group 2 (n = 63)	Group 3 (n = 39)	Group 4 (n = 69)	F	P-value
Diet Concern	-0.321 c	-0.874 d	0.396 b	1.495 a	199.957	0.000**
Weight fluctuations	-0.549 c	0.807 b	1.871 a	-0.219 c	229.211	0.000**

**Significant at 1%. Letters in horizontal orientation indicate statically significant differences according to Dunnett’s T3 Comparison test ($p \leq 0,001$), for non-homogeneous variables.

Table III						
Average scores fort he SWLS and SWFL scales and number of days with mental health problems in groups obtained by cluster analysis in university students from various regions in Chile, August 2013						
	Group 1 (n = 198)	Group 2 (n = 63)	Group 3 (n = 39)	Group 4 (n = 69)	F	P-value
SWLS	21.74 a	18.01 b	16.25 c	20.42 a	3.992	0.007*
SWFL	19.13 a	16.25 b	13.41 c	18.25 a	3.304	0.005*
Days with mental health problems	5.72 b	6.57 b	11.44 a	11.14 a	11.391	0.000**

*Significant at 5%.

**Significant at 1%.

Letters in horizontal orientation indicate statically significant differences according to Dunnett’s T3 Comparison test, for non-homogeneous variables.

Table IV
Characteristics (%) with statistically significant differences in groups of university students from various regions of Chile obtained by cluster analysis, August 2013

	Group 1 (n = 198)	Group 2 (n = 63)	Group 3 (n = 39)	Group 4 (n = 69)
<i>Gender</i>				
Male	49.5	58.7	56.4	20.3
Female	50.5	41.3	43.6	79.7
<i>Importance of eating habits for well-being</i>				
Not important at all	0.2	1.6	0.2	0.2
Very little important	3.8	3.2	2.4	0.2
Slightly important	10.1	22.2	7.7	2.5
Important	34.3	27.0	33.3	24.6
Very important	39.9	31.7	43.6	43.5
Totally and completely important	11.6	14.3	12.8	29.0

P values obtained by Chi² test.

weight fluctuations” (10.6%): scored high in DC, although significantly lower than Group 4. The WF score was significantly higher than in the remaining groups (table III). Scores on the SWLS and SWFL were significantly lower than in the other groups. Similarly, participants in Group 3 had the highest average number of days affected by mental health problems, though this did not differ statistically from Group 4 (table IV). This group consisted of a higher proportion of students who consume alcoholic beverages weekly (38.5%), restrict salt intake for health reasons (15.4%) and consumption of fried and fatty foods to prevent disease (53.8%) (table V).

Group 4 “Satisfied with life, moderately satisfied with their food-related life, concerned about dieting” (18.7%): this group had a significantly higher DC score than other groups. The score on WF was low (table II). It did not differ statistically from Group 1 in the scores of the SWLS and SWFL, and from Group 3 in the number of days affected by mental health problems (table III). This group was composed of a higher proportion of women (79.7%) and it considered that food is totally and completely important for their well-being (29.0%) (table IV). It also consisted of a higher proportion of students who consumed alcoholic beverages only occasionally (56.5 %), restricted sugar intake due to health reasons (14.5%) and to prevent disease (34.8 %), and restricted fried and fatty foods for the same reasons (14.5 and 47.8 %, respectively), restricted the consumption of pasta and rice due to health problems (14.5%) and alcohol to prevent disease (29.0%) (table V).

The types did not differ in mean BMI [Group 1 = 23.4 kg/m² (SD = 3.3); Group 2 = 23.7 kg/m² (SD = 3.9); Group 3 = 23.7 kg/m² (SD = 3.1), Group 4 = 23.1 kg/m² (SD = 2.7)]. According to the RRS scores and median, 32.8% of students in Group 1 correspond to chronic dieters; in Group 2 this figure reaches 42.9%, while in both Groups 3 and 4 100% of students may be considered chronic dieters.

Discussion

The results support a two-factor structure for the RRS in a sample of university students of both genders from various regions in Chile. Based on the scores on these two components of the RRS, Diet Concern and Weight Fluctuations, four student types were distinguished and characterized by their levels of life satisfaction and satisfaction with food-related life, number of days affected by mental health problems, importance given to food for personal well-being and certain eating habits. The most frequent type (Group 1, 53.8%) reported low concern for dieting and weight fluctuation. The second type (Group 2, 17.1%) reported concern about weight fluctuation, while the third type (Group 3, 10.6%) reported concern over both aspects, and the fourth one (Group 4, 18.7%) showed high concern over dieting. A rather interesting finding is the fact that all four types contain chronic dieters based on the RRS scores, which suggests that there may be different types of chronic dieters, and not just dieters and non-dieters. However, the median for the RRS in this study was below than the medians reported in research on women only.^{25,29,30} While groups 3 and 4 stand out because 100% of the students in each one would classify as chronic dieters according to their overall RRS score, they clearly represent different types of dieters. The population of restrained eaters therefore seems to consist of two subpopulations:³² The first type comprises successful dieters, who are characterized by high restraint and low tendency toward overeating, thus having a low susceptibility toward failure of restraint.³² This type of dieter belongs in Group 4. The second type is made up of unsuccessful dieters, who are characterized by high restraint and high tendency toward overeating, thus having a high susceptibility toward failure of restraint,³² traits which belong to Group 3.

A greater presence of women in Group 4 is consistent with studies that indicate a higher dietary restraint

Table V
Eating habits (%) with statistically significant differences in groups of university students from various regions of Chile obtained by cluster analysis, August 2013

	Group 1 (n = 198)	Group 2 (n = 63)	Group 3 (n = 39)	Group 4 (n = 69)
<i>Frequency of consumption of alcoholic beverages</i>			<i>P = 0.001</i>	
2-3 times a week	5.6	4.8	2.6	1.4
Once a week	16.7	11.1	38.5	4.3
Occasionally	40.9	50.8	25.6	56.5
Does not consume	36.9	33.3	33.3	37.7
<i>Restriction on sugar consumption restriction</i>			<i>P = 0.000</i>	
No	71.2	66.7	46.2	27.5
Restraint over health problems	3.5	4.8	10.3	21.7
Restraint to avoid diseases	22.2	22.2	33.3	42.0
Restraints because I dislike it	3.0	6.3	10.3	8.7
<i>Restriction on pastry consumption</i>			<i>P = 0.000</i>	
No	77.8	65.1	59.0	47.8
Restraint over health problems	2.0	4.8	10.3	14.5
Restraint to avoid diseases	14.6	19.0	23.1	34.8
Restraints because I dislike it	5.6	11.1	7.7	2.9
<i>Restriction on salt consumption</i>			<i>P = 0.048</i>	
No	63.6	61.9	43.6	55.1
Restraint over health problems	3.0	7.9	15.4	7.2
Restraint to avoid diseases	29.8	23.8	38.5	29.0
Restraints because I dislike it	3.5	6.3	2.6	8.7
<i>Restriction on fried foods and fat consumption</i>			<i>P = 0.001</i>	
No	55.1	55.6	35.9	24.6
Restraint over health problems	7.6	4.8	5.1	14.5
Restraint to avoid diseases	30.3	33.3	53.8	47.8
Restraints because I dislike it	7.1	6.3	5.1	13.0
<i>Restriction on pasta and rice consumption</i>			<i>P = 0.000</i>	
No	94.4	88.9	79.5	75.4
Restraint over health problems	1.5	4.8	7.5	14.5
Restraint to avoid diseases	3.5	1.6	12.8	10.0
Restraints because I dislike it	0.5	4.8	0.2	0.1
<i>Restriction on alcohol consumption</i>			<i>P = 0.002</i>	
No	50.0	41.3	56.4	31.9
Restraint over health problems	3.5	7.9	7.7	5.8
Restraint to avoid diseases	12.1	28.6	5.1	29.0
Restraints because I dislike it	34.3	22.2	30.8	33.3
<i>Frequency of fruit consumption in between meals</i>			<i>P = 0.011</i>	
Never	20.2	16.7	15.4	13.2
Occasionally	53.9	68.3	48.7	42.6
Frequently	25.9	15.0	35.9	44.1

P values obtained by Chi² test.

in women than in men.^{4,17} Also, the higher proportion of men in Group 2 is in line with studies that indicate that men are less concerned about eating and weight than women,¹² although there is evidence that male students tend to increase their BMI more than their female counterparts.⁷

Contrary to reports in previous studies, which have shown that chronic dieters have a higher BMI than non-dieters,^{18,25} no significant differences in each type's BMI were found in this study. Also there were no differences found between years of attendance,

although the literature states that dietary restraint predicts weight gain over the first year of university attendance.¹³ Likewise, no differences were detected between universities. This should be a matter of concern, in the sense that students with dietary restraint seem to be present in several regions of the country. Thus this is a problem that must be approached cross-wise by both Education and Health authorities. The significant higher number of days with mental health problems in Groups 3 and 4 is consistent with studies that associate dietary restraint with a poor psycholog-

ical health.¹⁶⁻¹⁹ Indeed, greater weight concern is an important mediator of the development of depressive symptoms.¹⁹

Our study sheds new light on the relationship between life satisfaction and dietary restraint. Previous studies (though only with females) have reported lower life satisfaction for chronic dieters.^{17,20} However, in our study, Group 4, which consists only of restraint eaters, has a SWLS score which is at the same level as that of the unrestrained eaters in Group 1. This suggests that, of the two components of the RRS, it is mostly the weight fluctuations component that is associated with satisfaction with life. Successful restraint eaters, where dietary restraint is not accompanied by weight fluctuations, may hence be as satisfied with their life as non-restrained eaters. The discrepancy in the SWLS score between groups 3 and 4 also contradicts studies that indicate that mental health problems correlate negatively with life satisfaction.²³ One possible explanation is that distress and depression can increase eating in some people, particularly dieters, and inhibit eating in others.¹⁴ Therefore, it can be suggested that while students in Group 4 are reacting to mental health problems by eating less, students from Group 3 react the opposite way, using eating as a coping mechanism to reduce stress. Therefore, even though both groups are chronic dieters and report a similar number of days with mental health problems, the significant differences between SWLS scores for both groups can be attributed to the fact that students in one group can successfully maintain their weight (Group 4) while the others cannot (Group 3).

A similar situation is reflected in the differences in the SWFL scores. While Group 4 was moderately satisfied with their food-related life and has a mean score similar to the unrestrained eaters in Group 1, Group 3 is dissatisfied, which may also be associated with the subpopulation of dieters³² to which people in this group belonged. A remarkable aspect in those types with higher levels of satisfaction with food-related life (Groups 1 and 4), is that both had a greater presence of students who believe that food is "totally and completely important" to their well-being. This is consistent with previous research conducted in Chile, which relates satisfaction with life and with food-related life with eating habits inside and outside the home in university students.²¹ However, from these results it is possible to unveil the relationship between the importance that students place on their eating habits and their level of satisfaction in this respect, whether they are chronic dieters or not.

The levels of dietary restraint in all four student types were not related to the frequency of consumption of foodstuffs groups. Nonetheless, differences regarding consumption of alcohol were detected, and the most frequent consumption was found in Group 3. Because alcohol contains a significant number of nonessential calories,³³ it would be expected that restrained eaters would impose strict rules about

alcohol consumption and avoid consuming alcohol. However, paradoxically, research demonstrates that restrained eaters may be more likely than unrestrained eaters to use compensatory eating strategies when they consume alcohol,³⁰ which is what may be happening in Group 3.

An important result to highlight corresponds to differences in food restriction and the reasons for such restrictions. Research on food selection indicates that the two aspects that people consider most important in their everyday food choices are taste and health. Thus, it is possible that when selecting food to eat, the individual will experience conflict between choosing the tasty option and the healthy (low-calorie) option.³⁴ Although a previous study with university students in Southern Chile indicated that satisfaction with life and food-related life may be associated with hedonistic reasons for food consumption, more than for nutritional or health reasons,³⁵ the present results suggest that some students care to avoid eating foods that negatively affect their health and weight. This is evident in the reasons given by most students from Group 4 to restrict the consumption of sugar, pastries, fatty and fried foods, pasta and rice, and students from Group 3 to restrict the intake of salt and fatty and fried foods. It is also noteworthy that students in Group 4 eat healthy food like fruits as a snack between meals. By contrast, the high proportion of students from Group 1 that does not restrict the consumption of any food, indicate hedonistic reasons related to food choices, thus choosing tasty foods.

Therefore, the results of this study indicate that both students who are concerned about their diet and weight and those who are not can experience higher levels of satisfaction with life and food-related life. Lower levels of satisfaction, overall and in the domain of food, may be related to weight fluctuations more than to dietary concerns. Both situations would be independent of the number of days with mental health problems reported by students.

Limitations of this study include the non-probabilistic nature of the sample and its relatively small size, which does not allow generalization of the results. Also, all data were self-reported, thus responses may be affected by social desirability and recall or response bias. Another limitation of the study lies in asking only the frequency of food consumption and not the amount ingested; therefore, it is not possible to analyze the real nutritional contribution of their intake. Also, inquiries about types of diet and ideal weight were not considered. These aspects must be dealt with in future studies.

Our study employs a mixed gender sample. The fact that three items were omitted from the original RRS scale, which worked fine with a female only sample previously also in Chile, may indicate that the psychometric properties of the RRS scale may differ depending on the gender composition of the scale. This as well is a topic for future research.

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Caso clínico

Cianocobalamina inhalada; una alternativa terapéutica eficaz y segura

Matilde Bettina Mijares Zamuner, Víctor González, Ángel Abad, Miguel Perdiguero y Antonio Picó

Servicio de Endocrinología y Nutrición. Hospital General Universitario de Alicante. Alicante. España.

Resumen

La deficiencia de vitamina B₁₂ o cobalamina es un trastorno nutricional frecuente, cuyo diagnóstico y tratamiento precoz es importante, debido a que es una causa reversible de alteración de la hematopoyesis y desmielinización del sistema nervioso central. La ingesta insuficiente de dicha vitamina junto con las alteraciones anatómicas o funcionales del estómago, páncreas e íleon terminal son las causas asociadas al déficit. Presentamos tres casos clínicos de pacientes con deficiencia de cobalamina secundaria a malabsorción intestinal tras cirugía bariátrica, asociada a mecanismos autoinmunes y a enfermedad inflamatoria intestinal respectivamente, que condicionaba una falta de respuesta al tratamiento con cianocobalamina oral a altas dosis. Además presentaban contraindicación para la administración de cianocobalamina intramuscular por el uso de anticoagulantes orales. En dichos pacientes, el uso de una formulación de cianocobalamina inhalada proporcionó una adecuada absorción de la misma, normalización de las concentraciones séricas de cobalamina y sin la existencia de efectos secundarios.

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Palabras clave: *Cianocobalamina inhalada. Anticoagulación oral. Deficiencia de vitamina B₁₂.*

INTRANASAL CYANOCOBALAMIN; AN EFFECTIVE AND SAFE THERAPEUTIC ALTERNATIVE

Abstract

Vitamin B₁₂ or cobalamin deficiency is a common nutritional disorder, in which the early recognition and treatment is critical since it is a reversible cause of bone marrow failure and demyelinating nervous system disease. Insufficient intake of vitamin along with anatomical or functional disorders of the stomach, pancreas and terminal ileum are the most frequent causes of the deficit. We present three cases of patients with cobalamin deficiency secondary to intestinal malabsorption after bariatric surgery, in relation to autoimmune process and inflammatory bowel disease mechanisms respectively, which conditioned a lack of response to treatment with high-dose oral cyanocobalamin. They also had contraindication to intramuscular administration of cyanocobalamin by the use of oral anticoagulants. In such patients, the use of an inhaled formulation cyanocobalamin provides an adequate absorption, normalizing serum cobalamin and without the existence of side effects.

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Key words: *Cyanocobalamin inhaled. Oral anticoagulation. Vitamin B₁₂ deficiency.*

Introducción

La vitamina B₁₂ o cobalamina es esencial en la reproducción celular, la hematopoyesis, la síntesis de nucleoproteínas y la mielinización del sistema nervioso central. Tras su conversión en coenzima B₁₂ en los tejidos, participa además en dos reacciones bioquímicas fundamentales, la síntesis de metionina a partir de la homocisteína y la conversión de L-metilmalonil-CoA en succinil-CoA¹. Según estudios epidemiológicos, en

países industrializados, la deficiencia de cobalamina (DC) alcanza una prevalencia del 20% de la población, con un rango entre 5-60%, dependiendo de la edad de la población estudiada y la definición de deficiencia establecida². La medición en dos ocasiones de concentraciones séricas de cobalamina inferiores a 150pmol/L (200 pg/ml) es la definición de DC más usada en la literatura pero sigue sin existir un método de referencia para su análisis y algunos grupos defienden la determinación de metabolitos intermedios, como la homocisteína sérica o ácido metilmalónico, para confirmar el déficit¹.

El metabolismo de la cobalamina es complejo y requiere además de una ingesta dietética diaria adecuada, la integridad anatómica y funcional de estómago, páncreas e íleon terminal, pudiendo existir DC en el caso de que cualquiera de ellos esté alterado¹. Sin embargo, debido al importante depósito hepático (1-

Correspondencia: Matilde Bettina Mijares Zamuner.
Servicio de Endocrinología y Nutrición.
Hospital General Universitario de Alicante.
Av. Maestro José Garberí, 14, Bloque I, Escalera 2, 7º AD.
03540 Alicante. España.
E-mail: matildex@hotmail.com

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2mg), se estima que entre el inicio de DC y la aparición de manifestaciones clínicas hay un periodo mínimo de cinco años. La sintomatología asociada incluye manifestaciones digestivas, neuropsiquiátricas o hematológicas con una gravedad variable, desde una glositis, parestias o macrocitosis aislada hasta una mielopatía o pancitopenia graves¹.

El tratamiento clásico de la DC es parenteral mediante inyecciones intramusculares o por vía oral con dosis altas de cianocobalamina, un análogo sintético de la cobalamina. El problema radica en pacientes que presentan contraindicaciones para la inyección intramuscular y asocian alteraciones anatómicas y funcionales digestivas que condicionan una falta de absorción o intolerancia de la vitamina por vía oral. A continuación se describen tres casos clínicos de pacientes con múltiples patologías que precisaron recibir cianocobalamina inhalada, como una alternativa eficaz y segura para el tratamiento de la DC.

Casos clínicos

Caso 1

Varón de 64 años intervenido de bypass gástrico de asa larga por antecedente de obesidad extrema. Precisa reintervención a los tres años para mayor alargamiento del asa alimentaria por ganancia ponderal, dejando asa común final de 90 cm. Como complicaciones secundarias presenta malabsorción con síndrome diarreico asociado, mala digestión por insuficiencia pancreática exocrina y sobrecrecimiento bacteriano. Todo ello condiciona anemia ferropénica grave, deficiencia de vitaminas liposolubles, folato y cobalamina (122 y 144 pg/ml; valores referencia 200-950 pg/ml [inmunoanálisis quimioluminiscente con analizador DxI de Beckman]). En el seguimiento es diagnosticado de fibrilación auricular crónica (FA) precisando anticoagulación oral con acenocumarol, y sustituyendo el tratamiento intra-

muscular quincenal de 1.000 µg de cianocobalamina a vía oral con una dosis diaria de 1.500 µg. Ante la progresiva disminución en la concentración de cobalamina alcanzando valores mínimos de 79 pg/ml, sin clínica asociada, se inicia tratamiento con 500 µg semanales de cianocobalamina intranasal objetivando aumento progresivo en la concentración de cobalamina (fig. 1).

Caso 2

Varón de 73 años con antecedente de síndrome de Sjögren y lupus eritematoso sistémico con glomerulonefritis proliferativa difusa en remisión completa y mononeuropatía sensitivo-motora múltiple diagnosticada con electromiografía por clínica de parestias y disminución de fuerza muscular en extremidades inferiores. Asocia FA paroxística, anticoagulante lúpico de alta potencia y anticuerpos antifosfolípidos, precisando anticoagulación con acenocumarol. Presenta ingreso hospitalario por deterioro de la función renal y alteraciones en la marcha. Se determina anemia normocítica normocrómica, concentraciones de cobalamina 135 y 155 pg/ml con anticuerpos anticelulas parietales negativos. Se inicia tratamiento con 1.000 µg diarios de cianocobalamina oral sin mejoría ni en la concentración sérica de cobalamina ni en la clínica del paciente, por lo que se inicia aporte de 500 µg semanales de cianocobalamina intranasal, con ascenso paulatino de la concentración de cobalamina y mejoría progresiva de la sintomatología neurológica (fig. 1).

Caso 3

Mujer de 65 años con antecedente de enfermedad de Crohn intervenida de hemicolectomía derecha y resección de válvula ileocecal, desnutrición calórica secundaria, deficiencia de vitamina D con osteopenia e insuficiencia renal crónica. Precisa además anticoagulación

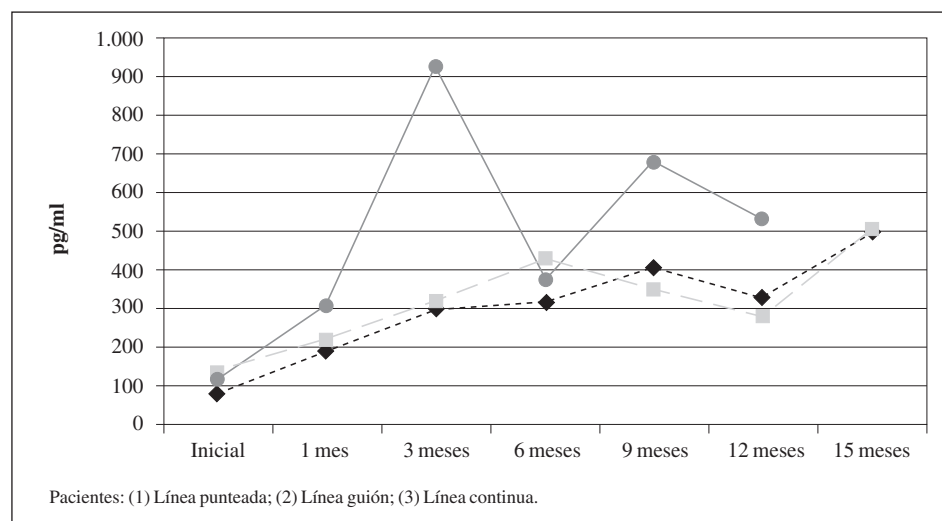


Fig. 1.—Determinación mensual y luego trimestral de las concentraciones séricas de cobalamina tras inicio de tratamiento con cianocobalamina inhalada.

oral por antecedente de FA y recambio valvular mitral y aórtico con prótesis mecánicas. Es diagnosticada de DC con concentraciones de cobalamina 147 y 120 pg/ml, sin clínica asociada, iniciando tratamiento con cianocobalamina oral a dosis de 1500 µg diarios, que es preciso suspender por intolerancia gastrointestinal con clínica de náuseas y diarrea. Se pauta tratamiento de 500 µg semanales de cianocobalamina intranasal, alcanzando progresivamente el rango de normalidad en la concentración sérica de cobalamina (fig. 1).

Discusion

La cianocobalamina inhalada se ha postulado como una opción terapéutica en los pacientes con DC que presentan contraindicación para la administración parenteral y/o intolerancia al tratamiento por vía oral o malabsorción que condiciona una falta de respuesta al mismo. La ruta metabólica de la cianocobalamina inhalada es similar a la administración parenteral, con una adecuada absorción a través de la mucosa nasal y una biodisponibilidad de la cianocobalamina inhalada con respecto a la intramuscular del 6,1% según estudios farmacocinéticos. En los tres casos clínicos referidos, el tratamiento con acenocumarol contraindicó la inyección intramuscular por el riesgo de hematomas y además asocian múltiples patologías que dificultan el mantenimiento de un rango terapéutico adecuado de anticoagulación³.

La malabsorción de cobalamina puede ser secundaria a un daño estructural o funcional del estómago, como sucede en pacientes gastrectomizados, debido a que las células parietales gástricas son las productoras del factor intrínseco (FI), proteína indispensable para la absorción de la vitamina en el íleon terminal. La DC también puede atribuirse a la insuficiencia pancreática exocrina que conduce a la ruptura inadecuada en el duodeno del complejo que une la cobalamina a haptocorrina, proceso necesario para su unión al FI y posterior absorción^{1,4}. Ambas condiciones favorecieron el desarrollo de DC y la falta de respuesta a cianocobalamina oral en el primer caso presentado.

Además de la afectación gástrica y pancreática, la DC puede ser debida a un daño en el lugar de absorción de la misma, el íleon terminal, específicamente los últimos 80 cm. Los pacientes afectados de enfermedad de Crohn o sometidos a resecciones ileales, cofactores en el caso del tercer paciente, o con sobrecrecimiento bacteriano, cofactor en el primer paciente, pueden presentar DC. Sin embargo, menos del 5% de la absorción de la cobalamina se realiza en su forma libre por difusión pasiva por lo que, teniendo en cuenta la capacidad de compensación del intestino no afecto, algunos pacientes pueden ser tratados por vía oral a dosis máximas⁵.

Los pacientes con enfermedades crónicas reumatológicas autoinmunes, como sucede en el segundo caso, desarrollan deficiencias de vitaminas y hierro secundarias a la malabsorción en relación con mecanismos

autoinmunes, existiendo una correlación inversa entre los niveles de cobalamina y la duración y actividad de la enfermedad reumatológica⁶. Por otra parte, en los tres pacientes presentados, el tratamiento prolongado con inhibidores de la bomba de protones (IBP) actuó como cofactor en la DC, debido a la supresión en la producción ácida de las células parietales y posterior descenso en la secreción del FI.

Las manifestaciones neurológicas, hematológicas y digestivas asociadas a DC son potencialmente graves por lo que en aquellos pacientes que presentan la deficiencia o estén en riesgo de desarrollarla es preciso su diagnóstico, monitorización y tratamiento¹. Según las últimas guías clínicas de tratamiento nutricional en pacientes sometidos a cirugía bariátrica, se debe realizar una determinación sistemática de las concentraciones de cobalamina por el riesgo de desarrollar DC. En estos pacientes, se puede utilizar la suplementación oral a dosis iguales o mayores a 1.000 µg diarios o administración intranasal 500 µg semanales, dejando la suplementación parenteral de vitamina B₁₂ a dosis 1.000 µg mensuales si fracasan las otras vías⁷. La cianocobalamina inhalada también se ha propuesto recientemente como alternativa terapéutica en aquellos pacientes en tratamiento crónico con IBP, porque permite un incremento seguro en las concentraciones séricas y una disminución en la frecuencia de DC⁸. Pero el uso de cianocobalamina intranasal se ha empleado de forma eficaz y con adecuada tolerancia, desde la década de los 50, para el tratamiento de los pacientes con anemia perniciosa^{9,10}. Dicha anemia es actualmente la causa más prevalente de DC grave a nivel mundial, y es debida a una gastritis atrófica autoinmune con pérdida del FI^{1,9}.

En los tres casos clínicos presentados, el tratamiento con cianocobalamina intranasal consiguió normalizar las concentraciones séricas de cobalamina y asoció mejoría en la clínica neurológica del segundo paciente, sin presentar en ninguno de ellos efectos secundarios. Para su administración se emplea un atomizador comercializado de cianocobalamina (500 µg/0,1 ml), con una dosificación de 500 µg, una aplicación semanal, alternando fosas nasales. La monitorización del tratamiento precisa determinación mensual de concentraciones séricas de cobalamina hasta alcanzar un valor normal, y posteriormente trimestrales.

Por tanto, aunque las vías parenteral y oral continúen desempeñando un papel importante en la DC, la administración semanal de cianocobalamina intranasal es una vía perfectamente aplicable de administración de cobalamina cuando exista un trastorno funcional o anatómico de aparato digestivo y por otra parte, esté contraindicada o el paciente la prefiera evitar la vía intramuscular.

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IN MEMORIAM

JUAN VOLTAS BARÓ (1931-2014)

Ex presidente de SENPE

Ha muerto en Pamplona el pasado 27 de junio, a la edad de 82 años, Juan Voltas Baró. Voltas fue presidente de la Sociedad Española de Nutrición Parenteral y Enteral (SENPE) en 1982; Organizó en Pamplona la Segunda Reunión de SENPE aquel año y fue elegido miembro de honor de la Sociedad.

Nacido en 1931 en Barcelona, Voltas Estudió Medicina en la Universidad Central de Barcelona formándose posteriormente en la Escuela del Profesor Piulachs. Compaginó los estudios con su actividad como prestidigitador, campo en el que alcanzó un notable prestigio. Sus habilidades lo hacían especialmente popular y querido por los enfermos, siempre sorprendidos. Cirujano hábil, de depurada técnica, se dedicó especialmente a la cirugía biliar y esófago-gástrica.

En 1956, Juan Voltas se traslado a Pamplona para contribuir a poner en marcha lo que sería la Facultad de Medicina de la Universidad de Navarra, formando parte de los pioneros de la Facultad de Medicina, de la Escuela de Enfermería y de la Clínica de la Universidad de Navarra. Inicialmente impartió la



Juan Voltas y su esposa, María Dolores Jurado, en el II Congreso de SENPE (Léon, 1985).

asignatura de Anatomía. Hasta 1969 ejerció la medicina privada en el Hospital San Juan de Dios de Pamplona.

Durante 22 años (1970-1992) fue profesor catedrático-ordinario de Cirugía y director del Departamento de Cirugía General y Digestiva, adaptándose siempre a los cambios ocurridos en el campo de la cirugía, implantando las subespecialidades quirúrgicas: cirugía colorectal, hepatobiliopancreática y trasplante hepático, endocrina, esófago-gástrica y patología mamaria. Voltas fundó a

principio de los noventa la revista Cirugía Iberoamericana.

Voltas formó a numerosos especialistas en cirugía general de renombre en Navarra y en España.

Casado con María Dolores Jurado, medico experta en nutrición, tuvieron cinco hijos y quince nietos.

Descanse en Paz, Juan Voltas Baró

Jesús M. Culebras

*Presidente de Honor de SENPE
Director de Nutrición Hospitalaria*